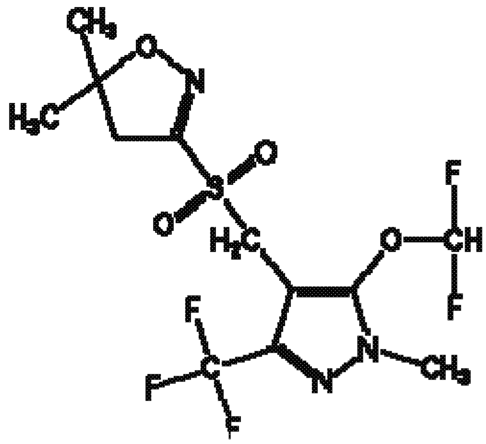
NEW CHEMICAL REGISTRATION
(Section 3)
ECOLOGICAL RISK ASSESSMENT
Pyroxasulfone: Herbicide
USEPA PC # 090099



Chemical Name(s): 3-[[[5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-4-yl]methyl]sulfonyl]-4,5-dihydro-5,5-dimethylisoxazole (CAS)
5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)pyrazol-4-ylmethyl 4,5-dihydro-5,5-dimethyl-1,2-oxazol-3-yl sulfone
Or
3-[5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)pyrazol-4-ylmethylsulfonyl]-4,5-dihydro-5,5-dimethyl-1,2-oxazole
(IUPAC)

Chemical Abstracts Service (CAS) Number: 447399-55-5

Chemical Family: Oxazole herbicide, pyrazole herbicide

Pesticidal Mode of Action: Sulfonylioxazoline (acetolactase synthase, ALS inhibitor); Inhibits biosynthesis of very-long-chain fatty acids (VLCFAs)[1]; K3 group of herbicides

Proposed End-use Product: Pyroxasulfone 85 WG (85% a.i.; EPA Reg.No.63588-xx)[a]; V-10233 Herbicide (42.5% pyroxasulfone; 33.5% flumioxazin)[b] water dispersible granule; Pyroxasulfone Technical (99.2% a.i.; EPA Reg No. 63588-xx) for formulation only into registered end-use herbicide products;

Target Pest(s): Weeds

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[1] Shimizu., T., Y. Tanetani, K.Kaku, K. Kawai, and T. Fujioka. 2009. Action mechanism of a novel herbicide, pyroxasulfone. *Pesticide Biochemistry and Physiology*, Vol. 95, Issue 1, p. 47-55. (also submitted as MRID 47701754)

Proposed Target Crop(s): [a]Field corn, popcorn, sweet corn, soybeans, winter wheat; [b]field corn, soybean, fallow land, non-crop areas around farms, orchards and vineyards and to maintain bare ground on non-crop areas

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I. Executive Summary

A. Nature of the Chemical Stressor

Pyroxasulfone is a new pesticide active ingredient being proposed as an herbicide to control weeds in various use sites (field corn, popcorn, sweet corn, soybeans, winter wheat; fallow land, non-crop areas around farms, orchards and vineyards and to maintain bare ground on non-crop areas). It is in the pyrazole class; also considered an oxazole, K-3 herbicide, and a sulfonylioxazoline (acetolactase synthase, ALS inhibitor). What is known is that the chemical inhibits biosynthesis of very-long-chain fatty acids (VLCFAs) - that are contained in the plasma membrane of plant cells - by preventing fatty acid precursors (medium- and long-chain fatty acids, which are formed in the chloroplast) from elongating into chains (in the endoplasmic reticulum). Ultimately, this effect leads to inhibition of plant shoot growth. Weedy species such as barnyard millet and Italian ryegrass, but also rice were determined to be sensitive to pyroxasulfone; wheat and corn to a lesser degree (Shimizu *et al.* 2009 MRID 47701754). It is unclear at this time to what degree the mechanism of VLCFA formation in animal cells might be affected as a result of exposure to pyroxasulfone.

The maximum single application rate of pyroxasulfone is 0.2136 lbs ai/A with a seasonal maximum rate of 0.267 lbs ai/A. Pyroxasulfone can be applied using broadcast or banded ground spray as well as aerial spray. Application timing is pre- and early post emergent. Other recommended applications include fall treatment (before ground freeze) and through dry fertilizer treatments. Depending on the crop, the recommended crop rotation intervals range 4 to 12 months. Several end-use products have been proposed including: Pyroxasulfone 85 WG (85% a.i.; EPA Reg.No.63588-xx); V-10233 Herbicide (42.5% pyroxasulfone; 33.5% flumioxazin) water dispersible granule; Pyroxasulfone Technical (99.2% a.i.; EPA Reg No. 63588-xx) for formulation only into registered end-use herbicide products.

B. Potential Risks to Non-target Organisms

The results of this screening-level assessment indicate a potential for direct adverse effects to non-target aquatic (non-vascular and vascular RQs of 1.03-22.07) and terrestrial plants (monocots in semi-aquatic areas RQs 1.35-1.75 exceed listed species LOC), birds (chronic dietary-based RQ 1.07) and mammals (chronic dose-based RQs 1.17-3.86) following chronic exposure. Due to the potential for direct adverse effects to aquatic/terrestrial plants, birds, and mammals associated with the application of pyroxasulfone on corn, soybean, winter wheat, and non-crop sites, indirect effects may consequently affect other aquatic and terrestrial species. Data were not submitted for the marine/estuarine fish and invertebrates via chronic exposure. Without data, risk cannot be ruled out for these taxa (either non-listed or federally listed species) with certainty. However, this assessment assumes that estuarine/marine organisms are of comparable sensitivity to pyroxasulfone as freshwater organisms are, which implies that risk to estuarine/marine organisms from chronic exposure to pyroxasulfone is not expected. Metabolite/degradate data were submitted only for non-vascular and vascular aquatic plants and mammals (acute oral studies). With the exception of two terrestrial plant studies and two non-guideline terrestrial invertebrate studies, no data using formulations of pyroxasulfone were submitted leading to uncertainty in the assessment of risk for end use products. This does not affect the conclusions made on the technical grade active ingredient and metabolites (where available).

Table 1. Summary of Environmental Risk Conclusions for Aquatic Animals and Plants from Proposed Pyroxasulfone Uses

Taxonomic Group	Assessment Endpoint	Summarized Risk Characterization and Important Uncertainties
Freshwater Fish and Aquatic Phase Amphibians	Mortality	Acute risk is not expected.
	Growth (wet wt, length)	Chronic risk is not expected.
Freshwater Invertebrates	Immobility	Acute risk is not expected.
	Reproduction, growth, survival	Chronic risk is not expected.
Marine/ Estuarine Fish	Mortality	Acute risk is not expected.
	Reproduction, growth etc.	No studies submitted. Chronic risk not expected.
Marine/ Estuarine Invertebrates	Mortality	Acute risk is not expected.
	Reproduction, growth etc.	No studies submitted. Chronic risk not expected.
Aquatic Plants	Growth (frond count[1] , cell density[2])	Risk is expected (from the technical grade active ingredient, but not the metabolites).

* Consult 'Risk Description' section for further details. Also, risk in this table implies risk to technical grade active ingredient unless otherwise specified that metabolites and/or formulations were assessed as well.
[1] Vascular plants
[2] Non-vascular plants

Table 2. Summary of Environmental Risk Conclusions for Terrestrial Animals and Plants from Proposed Pyroxasulfone Uses		
Taxonomic Group	**Risk Endpoint**	**Summarized Risk Characterization and Important Uncertainties**
Birds, Reptiles and Terrestrial Phase Amphibians	Mortality	Acute risk is not expected.
	Reproduction (hatchability)	Chronic risk <u>is expected.</u>
Mammals	Mortality	Acute risk is not expected (from technical grade active ingredient, metabolites/degradates, or formulated products WG85 and V-10233).
	Growth (body wt gain)	Chronic risk <u>is expected</u>.
Non-target Invertebrates	Mortality	Acute risk to honeybees is not expected (from technical grade active ingredient). Acute and chronic[1] risk to earthworms (from technical grade active ingredient) and acute risk to terrestrial invertebrates (non-gln) is not expected (from formulated product WG85).
Terrestrial Plants	Growth (length or height, weight)	Risk to terrestrial plants <u>is expected</u> (based on EUP).
* Consult 'Risk Description' section for further details. Also, risk in this table implies risk to technical grade active ingredient unless otherwise specified that metabolites and/or formulations were assessed as well. [1] In addition to mortality, other endpoints considered in the earthworm reproduction and growth study include body wt loss and juvenile counts		

C. Environmental Fate Summary

Pyroxasulfone is mobile (K_{oc}= 57-119 L/kg) and persistent ($t_{1/2}$= 142 to 533 days) in terrestrial and aquatic environments. The major routes of dissipation are expected to be associated with microbial-mediated degradation, leaching, and runoff. Pyroxasulfone is stable to hydrolysis and photodegradation in water and soil. Volatility is not expected to be a major dissipation pathway because of the low vapor pressure ($1.8E^{-8}$ torr) and Henry's Constant ($2.65E^{-9}$ atm-m3/mole). Also, the bioaccumulation potential of pyroxasulfone is expected to be low due to a low octanol: water coefficient (log Kow=2.39). Field dissipation studies indicate rapid dissipation ($t_{1/2}$= 4 to 35 days) of pyroxasulfone. Degradation of pyroxasulfone was identified as a potential route of dissipation in field studies. Leaching also was identified as a route of dissipation of the metabolite 5-difluoromethoxy-1H-pyrazol-4-yl) methanesulfonic acid (M1). This degradation product was very persistent (extrapolate $t_{1/2}$~ 8 to 65 years) in laboratory metabolism studies.

Another major degradation product (present at ≥10% applied radioactivity) was identified as 5-difluoro methoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M3). Minor degradation products (<10% of applied radioactivity) of pyroxasulfone are:

- 3-(5-Difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazole (M5),
- 3-(5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazol-4-ol (M6),
- (5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl) methanol (M8),

- 5-difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M9),
- 5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carbaldehyde (M10), and
- [3-5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-(ylmethanesulfonyl)-4,5-dihydro-5-methylisoxazol-5-yl] methanol (M11).

The Residue of Concern Knowledgebase Subcommittee (ROCKS) in the Office of Pesticide Programs (OPP) identified pyroxasulfone, M1, and M3 as residues of concern in the human health risk assessment.

Additionally, there was a high percentage of applied radioactivity (8-25% of applied radioactivity) in "unextracted" soil/sediment residues. Because the extraction of pyroxasulfone residues was conducted using only acetonitrile/water without the use of sequentially harsher extractants, there is uncertainty regarding the identity and availability of the unextracted soil residues.

D. Ecological Effects Summary

Aquatic Animals

<u>Acute</u>

Freshwater and marine/estuarine fish were tested on the technical grade active ingredient and did not show (sub)lethal effects at limit concentrations (2.2 mg a.i./L for rainbow trout, MRID 47701626; 2.8 mg a.i./L for bluegill sunfish, MRID 47701627) or up to the highest concentration tested (3.3 mg a.i./L for sheepshead minnow, MRID 47701628); LC_{50} values indicate that pyroxasulfone is at most moderately toxic to freshwater and estuarine/marine fish.

Similarly, the freshwater and estuarine/marine invertebrates were tested on the technical grade active ingredient and did not show (sub)lethal effects at the limit concentration (4.4 mg a.i./L for water flea, MRID 47701623) or up to the highest concentration tested (3.6 mg a.i./L for eastern oyster, MRID 47701624; 1.4 mg a.i./L for saltwater mysid, MRID 47701625); EC_{50} values indicate that pyroxasulfone is at most moderately toxic to freshwater and marine/estuarine invertebrates.

<u>Chronic</u>

Unlike the acute toxicity study which lead to a non-definitive endpoint, the chronic toxicity study using the technical grade active ingredient on freshwater fish determined a definitive endpoint (28-day NOAEC of 2.0 mg a.i./L for fathead minnow, MRID 47701630) on the basis of wet weight and length (growth endpoints) reductions at the highest concentration tested (3.9 mg a.i./L).

A chronic freshwater invertebrate study using the technical grade active ingredient determined a non-definitive endpoint (NOAEC $\geq$1.9 mg a.i./L for water flea, MRID

47701629) given that differences between treatment groups and controls were not statistically significant and sublethal effects (discoloration, injury, and lethargy) were infrequent, comparable to controls, and not considered treatment related.

Chronic toxicity studies on the marine/estuarine fish and invertebrates were not submitted by the registrant.

Aquatic Plants
The vascular aquatic plant data on the technical yielded a definitive endpoint (7-day EC_{50} of 6.0 µg a.i./L, NOAEC of 0.18 µg a.i./L for duckweed, MRID 47701640) on the basis of frond count; however, two studies on the metabolites (M-1, M-3) indicated that none of the endpoints of interest (frond count, biomass, growth rate) were affected leading to a non-definitive endpoint for both studies (7-day EC_{50} > 123 mg a.i./L, NOAEC ≥123 mg a.i./L, MRIDs 47701641, 47701642). Chlorosis and necrosis were consistently observed in all three studies.

On the other hand, three non-vascular aquatic plant studies on the freshwater green algae yielded definitive endpoints for the technical (96-hr EC_{50} of 0.00038 mg a.i./L, NOAEC of 0.0001 mg a.i./L, MRID 47701643), metabolite M-1 (96-hr EC_{50} of 56 mg a.i./L, NOAEC of 31 mg a.i./L, MRID 47701647), and metabolite M-3 (96-hr EC_{50} of 38 mg a.i./L, NOAEC of 15 mg a.i./L, MRID 47701648). In all three studies, all three endpoints of interest (cell density, biomass, and growth rate) were affected, with cell density generally being the most sensitive of the three endpoints; however, no sublethal effects were observed. Similarly, the marine diatom indicated sensitivity to the technical grade active ingredient yielding a definitive endpoint for the most sensitive endpoint, cell density (96-hr EC_{50} of 0.66 mg a.i./L, NOAEC of 0.14 mg a.i./L, MRID 47701646), though all three endpoints of interest were affected and cell aggregation (apparently a symptom at relatively high cell densities) was observed in all treatment levels. The freshwater blue-green algae on the technical yielded a non-definitive EC_{50} for all three endpoints, but on the basis of the NOAEC (0.16 mg a.i./L, MRID 47701644), cell density and growth rate were deemed most sensitive and biomass less so (NOAEC 1.6 mg a.i./L). Cell aggregation and long chains were observed in all treatment levels and controls. Finally, the freshwater diatom indicated no sensitivity to the technical whereby the cell density, biomass, and growth rate endpoints were all non-definitive (96-hr EC_{50} >3.2 mg a.i./L, NOAEC ≥ 3.2 mg a.i./L, MRID 47701645) and cell aggregation was observed in all treatment levels and controls.

Terrestrial Animals
<u>Acute</u>
Upland, waterfowl, and passerine birds were tested on the technical grade active ingredient. The acute oral studies did not show (sub)lethal effects at limit concentrations (2250 mg a.i./kg-bw for zebra finch, MRID 47701632) or up to the highest concentration tested (2250 mg a.i./kg-bw for northern bobwhite quail, MRID 47701631); LD_{50} values indicate that pyroxasulfone is practically non-toxic to birds on an acute oral basis. An acute dietary study determined a non-definitive endpoint (8-day LC_{50}> 5620 mg a.i./kg-diet and NOAEC≥5620 mg a.i./kg-diet for northern bobwhite quail, MRID 47701633)

given that the study indicated no mortalities, overt signs of toxicity, or treatment-related effects on body weight or food consumption at the dosage levels tested; in addition, sublethal effects (leg lesions, limping, wing droop) were not considered treatment related. A second acute dietary study determined a non-definitive endpoint (8-day LC_{50}> 5620 mg a.i./kg-diet for mallard duck, MRID 47701634) given that the study indicated no mortalities, overt signs of toxicity, or treatment-related effects on food consumption at the dosage levels tested. However, relative to the control, the highest two treatment groups 3160 and 5620 mg a.i./kg-diet had a reduced increase in body weight that was significantly different from the control. The reductions in body weight increase led to a determination of an 8-day NOAEC of 1780 mg a.i./kg-diet (EPA calculation) and a 5-day NOAEC of 1000 mg a.i./kg-diet (APVMA calculation). The LC_{50} values from the acute dietary studies indicate that pyroxasulfone is practically non-toxic to birds on an acute oral basis

Eight acute oral studies were conducted on female rats to satisfy OCSPP guidance 870.1100 (OECD 425) – one technical and seven degradate/metabolite (M-1, M-3, M-25, I-3, I-4, I-5, M-28). All of the studies were deemed acceptable and indicated that the test compound was practically non-toxic with toxicity category III. However, all of the studies were conducted at a limit dose of 2000 mg a.i./kg-bw and without control groups. Two formulation studies were conducted on female rats to satisfy OCSPP guidance 870.1100 (OECD 425) – one on WG85 (85%a.i.) and one on V-10233 (42.2% pyroxasulfone; 33.6 flumioxazin). Both studies were limit tests and deemed acceptable; however, no control groups were used in the study design. The single active ingredient product tested (MRID 47701916) is at most slightly toxic (category III), while the co-formulated product (MRID 47702105) is practically non-toxic (category IV) at the respective limit doses. No deaths or sublethal effects were observed in either study.

Terrestrial Invertebrates

A 48-hour acute contact study using the technical grade active ingredient on the honey bee indicated no effect to mortality and sporadic sublethal effects such as lethargy, loss of equilibrium, and immobility. The compound is considered practically non-toxic to honey bees on the basis of a non-definitive endpoint (LD_{50} > 100 µg a.i./bee, MRID 47701637).

A couple non-guideline studies on formulation WG85 (84.7% purity) indicated effects to fecundity that did not reach a 50% reduction at any level of exposure (parasitization of aphids in parasitoid wasps, 48-hour ER_{50} and LR_{50} >0.892 lbs a.i./A, MRID 47889323) as well as mortality and fecundity that did reach a 50% reduction but was not deemed dose dependent (overall eggs produced per female predatory mite per day, 7-day ER_{50} and LR_{50} >0.892 lbs a.i./A, MRID 47701753).

Another couple of non-guideline studies using the technical grade active ingredient on the earthworm indicated no effects at the concentrations tested which resulted in non-definitive endpoints for the 14-day study (LC_{50} > 997 mg a.i./kg dry soil, MRID 47701748) and 28-day reproduction and growth study (NOAEC ≥ 1000 mg a.i./kg dry soil, MRID 47933801).

Chronic

Out of the two 1-generation reproduction studies for birds, mallard duck was more sensitive (NOAEC of 60 mg a.i./kg diet on the basis of biologically significant effect on hatchability, MRID 47701636) than the northern bobwhite quail (NOAEC $\geq$ 1000 mg a.i./kg diet on the basis of no apparent treatment related effects on adult or offspring body weight, reproductive performance, and eggshell thickness, MRID 47701635).

Out of four chronic mammalian studies available all on the technical grade active ingredient, the 2-generation reproduction study on the rat yielded the most sensitive endpoint (NOAEL of 7.2 mg/kg-bw/day for males on the basis of decreased body weight, body weight gain, and food consumption in the parent generation, MRID 47701706).

Terrestrial Plants

According to a registrant submitted open literature study (Shimizu *et al.* 2009, MRID 47701754), which identifies the mode of action of pyroxasulfone, also indicates that the chemical leads to an inhibition of shoot growth to monocots grown for 6-7 days from seed at concentrations on the order of $10^{-7} - 10^{-5}$M (80 to near 100% inhibition in rice, Italian ryegrass, and barnyard millet) and $10^{-6} - 10^{-5}$ M (approximately 25 to 75% inhibition for wheat) and to a much lesser extent at these concentrations for corn (less than 20% inhibition). The concentrations in solution 10^{-7}, 10^{-6}, and 10^{-5}M on a mass: volume basis equate to 0.04, 0.4, and 4 mg/L [ppm] (given that M = moles/L; concentration in M * 367 g/mol *10^3 mg/g) and 40, 400, and 4000 µg/L [ppb]. However, these concentrations exceed the aquatic EECs (maximum concentration calculated in PRZM/EXAMS is 8.4 µg/L, see Table 14) by at least an order of magnitude. The concentrations in solution 10^{-7}, 10^{-6}, and 10^{-5}M on a mass: mass basis equate to 0.00734, 0.0734, and 0.734 mg a.i./kg soil [ppm] (given that M = moles/L; concentration in M * 0.001 L/mL* 1mL/g H_2O * 367 g/mol *10^3 mg/g *20 g H_2O/100 g dry soil *100 * 1000g/1kg) and 0.015, 0.15, and 1.5 lbs a.i./A (mg a.i./kg soil * 2 million lbs soil in an acre 6 inches deep). The higher of these concentrations (0.15 and 1.5 lbs a.i./A) exceed the highest terrestrial plant EECs (0.02 and 0.03 lbs a.i./A, see Table 17) for semi aquatic areas given ground spray application at rates of 0.206 and 0.267 lbs a.i./A (respectively), but the lowest concentration (0.015 lbs a.i./A) is slightly below these terrestrial plant EECs, for which the listed LOC is exceeded for monocots in semi-aquatic areas. Similarly, the aerial application of 0.120 lbs a.i./A leads to a terrestrial plant EEC of 0.018 lbs a.i./A, a value comparable to the lowest concentration in the mode of action study (0.015 lbs a.i./A), for which the listed plant LOC is exceeded for monocots in semi-aquatic areas. These calculations imply that at the higher ground spray applications and the aerial application for one of the formulations, an effect on shoot growth is possible on target weeds Italian ryegrass, barnyard millet, but also on rice and potentially other non-target monocots. Furthermore, the seedling emergence study (MRID 47701638) indicated that wheat dry weight (MSD 41.21%) had the following percent reductions 22, 22, 12, 2.5, and 28% relative to the control which were not detected as statistically significant at 0.0168, 0.0334, 0.0669, 0.1338, and 0.2676 lbs a.i./A concentrations, respectively. This indicates that the study may not capture what it was intended to capture as there was high variability in the raw data. However, for wheat, this still implies that sublethal effects may be observed below maximum application levels (in the study as well the given labels) and below the lowest tested concentration.

Despite some limitations (on account of variability in the raw data) in detecting plant sensitivity to pyroxasulfone, the seedling emergence study led to identification of the most sensitive monocot (onion, EC_{25} of 0.0669 lbs a.i./A and NOAEC of 0.0168 lbs a.i./A) and dicot species (kidney bean, EC_{25} of 0.2615 lbs a.i./A [just below the highest concentration tested – i.e., 0.2676 lbs a.i./A] and NOAEC of 0.1338 lbs a.i./A) based on observed changes in length.

The vegetative vigor study (MRID 47701639), indicated that monocots, overall, did not exhibit signs of treatment-related toxicity, whereas dicots did. However, there is some uncertainty in these results considering that potential weeds or pest species are monocots (e.g., barnyard millet, Italian ryegrass). As a result determining the most sensitive monocot (*i.e.*, onion) was based on the lowest EC_{25} of the monocots for which the endpoint was available. However, the EC_x's for onion (as well as most monocot data) did not indicate convergence whereby an algorithm was not plotted against the data indicating clear inhibition with increasing concentration. As a result, for onion the $EC_{25} >$ 0.2676 lbs a.i./A (the highest concentration tested) and the NOAEC is equal to the highest concentration tested. On the other hand, the most sensitive dicot was the pumpkin (EC_{25} of 0.0748 lbs a.i./A and NOAEC of 0.0168 lbs a.i.A).

In addition, given that pyroxasulfone may leach into groundwater, predicted concentrations of pyroxasulfone (equivalent to the equilibrium concentration taken over a 30 year period) were used to estimate the potential phytotoxic effects from irrigation water to plants and sensitive crops on the treated field. If listed monocot and dicot species and/or sensitive crops are exposed on the treated field to the estimated amounts of pyroxasulfone in irrigation water, then effects will be expected.

Risk Conclusions

Based on the available ecotoxicity data and predicted environmental exposures, risks to aquatic (non-vascular and vascular, listed and non-listed) and terrestrial (listed) plants as well as listed and non-listed birds (as well as reptiles and amphibians) and mammals following chronic exposure are expected. In addition, risk to listed terrestrial plants and potentially sensitive crops located on the irrigated/treated field are expected as a result of use of pyroxasulfone contaminated irrigation water at the estimated levels. The pyroxasulfone degradates, M-1 and M-3, are not considered degradates of concern for duckweed (vascular aquatic plant) or freshwater green algae (non-vascular aquatic plant). The pyroxasulfone degradates, M-1, M-3, M-25, I-3, I-4, I-5, M-28, are not considered degradates of concern for mammals (on an acute basis). The formulations WG85 (84.7% a.i.) and V-10233 (42.2% pyroxasulfone; 33.6% flumioxazin) are not considered to pose a risk to mammals (on an acute basis). The formulation WG85 (84.7% a.i.) is considered to not pose a risk to (non-guideline) terrestrial invertebrates (parasitoid wasp, predatory mite).

E. Uncertainties and Data Gaps

1. Environmental Fate and Exposure

The submitted fate database is incomplete for pyroxasulfone on account of the need for ground water monitoring data. In addition, an uncertainty in the environmental fate data is the identification and availability of unextracted residues in soil and aquatic metabolism studies. These residues account for a high percentage of applied radioactivity (8-25% of applied radioactivity). Although there is an uncertainty regarding the identification and quantification of unextracted soil/sediment residues, this uncertainty does not substantially affect the estimated exposure levels due to the persistence of pyroxasulfone. For a list of submitted environmental fate studies for pyroxasulfone see SectionV.

Data needs:
Because pyroxasulfone is mobile and persistent in soil it has the potential to leach into groundwater. This behavior was predicted using Tier II PRZM GW model. This modeling showed that pyroxasulfone has the potential to accumulate in groundwater.

- Prospective ground water monitoring study.

2. Ecological Effects Data

The submitted ecotoxicity database is incomplete. For a list of submitted ecological effects studies for pyroxasulfone see Section V. The following studies are considered data gaps:

Chronic Marine/Estuarine Fish Study
No chronic studies on marine/estuarine fish were submitted by the registrant. Therefore, a quantitative estimation of risk could not be conducted. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is stable to hydrolysis (at pHs 4, 7, and 9) and aqueous photolysis (half life = 119 days), comparison to freshwater fish data suggests that chronic risk to marine/estuarine fish is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean wheat, and non-crop sites. Therefore, a chronic marine/estuarine fish study is not required.

- Chronic: Fish early-life stage (saltwater: *Cyprinodon variegatus*) (850.1400; 72-4), TGAI

Chronic Marine/Estuarine Invertebrate Study
No chronic studies on marine/estuarine invertebrates were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is stable to hydrolysis (at pHs 4, 7, and 9) and aqueous photolysis (half life = 119 days), comparison to freshwater invertebrate data suggests that chronic risk to marine/estuarine invertebrates is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean,

wheat, and non-crop sites. Therefore, a chronic marine/estuarine invertebrate study is not required.

- Chronic: Marine/estuarine invertebrate (*Americamysis bahia*) (850.1350; 72-4), TGAI

Fish Bioaccumulation Study

A bioaccumulation in fish study was not submitted to support the proposed registration. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is mobile and persistent, the low octanal:water partitioning coefficient (log K_{ow}= 2.39) is expected to limit bioconcentration and bioaccumulation of pyroxasulfone. Based on the log K_{ow} of 2.39, the expected BCF assuming no metabolism and 5% lipids would be approximately 12 L/kg wet weight (*i.e.,* $10^{2.39} * 0.05$). This low BCF combined with the low acute toxicity to birds and mammals indicates that risks to piscivorous wildlife would not be expected. Therefore, a fish bioaccumulation study is not required.

- Fish Bioaccumulation study (850.1730; 72-6, 165-4), TGAI

F. Endangered Species Considerations

Table 3 summarizes the listed species at risk associated with either direct or indirect effects following application of pyroxasulfone for the proposed uses.

Concerns For Federally Listed as Endangered and/or Threatened Species

Table 3. Listed Species Risks Associated With Direct or Indirect Effects from Pyroxasulfone use

Listed Taxon	Direct Effects	Indirect Effects
Terrestrial and semi-aquatic plants - monocots	Yes	Yes[4]
Terrestrial and semi-aquatic plants – dicots	No	Yes[4]
Terrestrial invertebrates	No	Yes[4]
Birds	Yes (chronic)	Yes[4]
Terrestrial-phase amphibians[1]	Yes (chronic)	Yes[4]
Reptiles[1]	Yes (chronic)	Yes[4]
Mammals	Yes (chronic)	Yes[4]
Aquatic non-vascular plants	Yes	Yes[4]
Aquatic vascular plants	Yes	Yes[4]
Freshwater (FW) fish	No	Yes[4]
Aquatic-phase amphibians[2]	No	Yes[4]
Freshwater (FW) invertebrates	No	Yes[4]
Marine/estuarine (M/E) fish	No[3]	Yes[4]
Marine/estuarine (M/E) invertebrates (mollusk)	No[3]	Yes[4]

[1] Results from birds used as surrogate for assessing risk to terrestrial-phase amphibians and reptiles
[2] Results from freshwater fish used as surrogate for assessing risk to aquatic-phase amphibians
[3] Assumption of no expected risk or direct effect is made on the basis of freshwater fish and invertebrate data.
[4] From effects to mammals, birds, plants

II. Problem Formulation

The purpose of this problem formulation is to provide the foundation for the ecological risk assessment being conducted for the herbicide pyroxasulfone. As such, it articulates the purpose and objectives of the risk assessment, evaluates the nature of the problem, and provides a plan for analyzing the data and characterizing the risk (EPA, 1998).

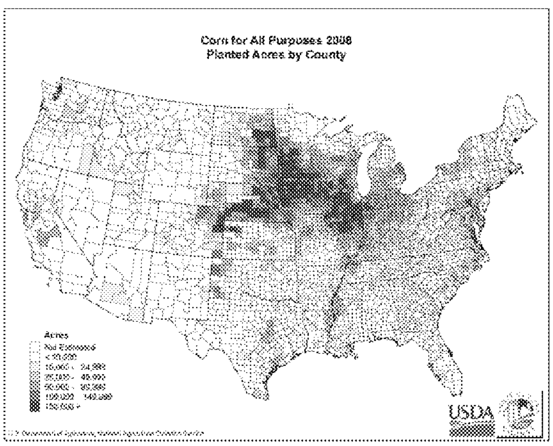
A. Nature of Regulatory Action

Pyroxasulfone is a new pesticide active ingredient being proposed as an herbicide to control weeds in various use sites (field corn, popcorn, sweet corn, soybeans, winter wheat; fallow land, non-crop areas around farms, orchards and vineyards and to maintain bare ground on non-crop areas). As a new active ingredient submitted for registration, there are no previously prepared ecological risk assessments by the Agency for pyroxasulfone uses. However, the chemical is undergoing a global review in which Australian Pesticides and Veterinary Medicines Authority, APVMA (Australia) and Pest Management Regulatory Agency, PMRA (Canada) have contributed to secondary review of fate and ecotoxicity studies.

B. Stressor Source and Distribution

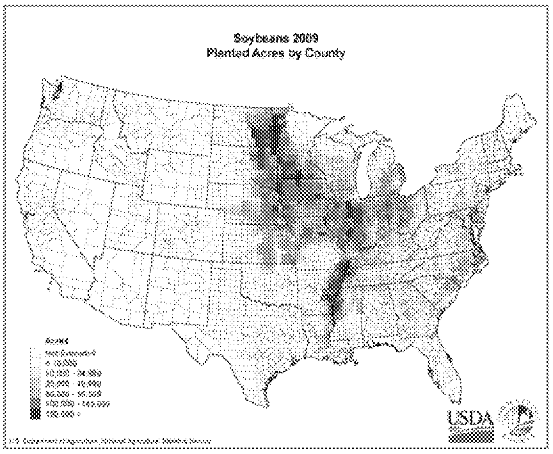
The proposed crop use sites are corn (sweet, field, popcorn), soybean, and winter wheat. Additionally, non-crop use sites include fallow land and non-crop areas around farms, orchards, and vineyards. Fallow land and crop use treatment requires consideration of rotation intervals because of the persistence of pyroxasulfone. Recommended rotation intervals into treated fields are 4 months for winter wheat, 8 months for spring wheat, 9 months for corn, sunflower, dry common beans, canola, 11 months for alfalfa, barley, canola, and 12 months for all other crops. The extent of potential crop use areas for pyroxasulfone are shown in **Figure 1**. The extent of non-crop uses cannot be spatially identified due to the generalized nature of the use pattern as well as the lack of adequate GIS overlays for non-crop use areas.

A) Corn



ED_005172C_00002001-00016

B) Soybean



C) Winter Wheat

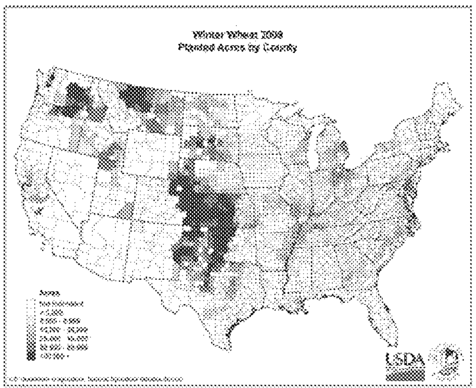


Figure 1: Potential Crop Use Areas for Pyroxasulfone
(From USDA 2008 and 2009 County Crop Programs available at: http://www.rma.usda.gov/data/cropprograms.html).

1. Nature of the Chemical Stressor

Figure 2 provides the chemical structure of pyroxasulfone. **Table 4** identifies the physical and chemical properties of pyroxasulfone from experimental data.

Figure 2. Chemical Structure of Pyroxasulfone

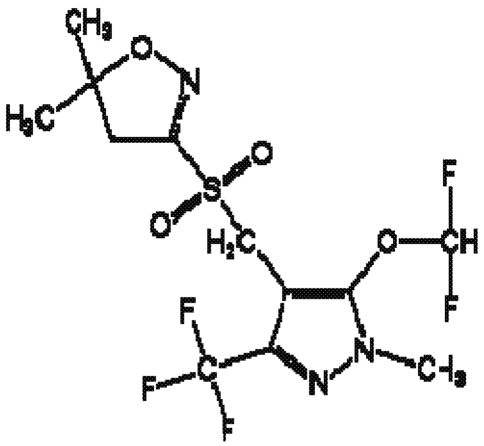


Table 4: Environmental Fate Properties of Pyroxasulfone	
PARAMETER	**VALUE**
Chemical and Physical Properties	
Chemical name(s)	3[(5-difluoromethoxy-1-methyl-3-trifluoromethylpyrazol-4-yl) methylsulfonyl]-4,5-dihydro-5,5-dimethylisoxazole
CAS Number	44739-55-5
Molecular Weight (grams/mole)	367 g/mole
Aqueous solubility (at 25°C)	3.49 mg/L
Vapor Pressure	1.8×10^{-8} torr
Henry's Law Constant	2.65×10^{-9} atm m^3/mol
Octanol Partitioning Coefficient (log K_{ow}) @25°C	2.39
Environmental Fate Properties	
Hydrolysis half life (pH 4, pH 7, pH 9)	Stable
Aqueous photolysis half life	119 days
Soil photolysis half life	Stable (>30 days)
Aerobic soil metabolism half-lives	142-533 days
Anaerobic soil metabolism half-lives	145 -156 days
Aerobic aquatic metabolism half-lives	108 -109 days*
Anaerobic aquatic metabolism half-lives	69-70 days*
Soil-water distribution coefficient (K_{oc})	57-119
* Calculated from combined residues of the test compound measured in both the aqueous and the soil/sediment phases of a given test system.	

Proposed End-use Products: Pyroxasulfone 85 WG (85% a.i.; EPA Reg.No.63588-xx); V-10233 Herbicide (42.5% pyroxasulfone; 33.5% flumioxazin) water dispersible granule; Pyroxasulfone Technical (99.2% a.i.; EPA Reg No. 63588-xx) for formulation only into registered end-use herbicide products.

a. Mode of Action (MoA) of Pyroxasuflone

Pyroxasulfone is a new herbicide in the pyrazole class; also considered an oxazole, K-3 herbicide, and a sulfonylioxazoline (acetolactase synthase, ALS inhibitor). What is known is that the chemical inhibits biosynthesis of very-long-chain fatty acids (VLCFAs) - that are contained in the plasma membrane of plant cells - by preventing fatty acid precursors (medium- and long-chain fatty acids, which are formed in the chloroplast) from elongating into chains (in the endoplasmic reticulum). Ultimately, this effect leads to inhibition of plant shoot growth. Weedy species such as barnyard millet and Italian ryegrass, but also rice were determined to be sensitive to pyroxasulfone; wheat and corn to a lesser degree (Shimizu *et al.* 2009 MRID 47701754). It is unclear at this time to what degree the mechanism of VLCFA formation in animal cells might be affected as a result of exposure to pyroxasulfone.

b. Environmental Fate Summary

Pyroxasulfone is mobile (K_{oc}= 57-119 L/kg) and persistent ($t_{1/2}$= 142 to 533 days) in terrestrial and aquatic environments (Table 3). The major routes of dissipation are expected to be associated with microbial-mediated degradation, leaching, and runoff. Pyroxasulfone is stable to hydrolysis and photodegradation in water and soil. Volatility is not expected to be a major dissipation pathway because of the low vapor pressure ($1.8E^{-8}$ torr) and Henry's Constant ($2.65E^{-9}$ atm-m^3/mole). Also, the bioaccumulation potential of pyroxasulfone is expected to be low due to a low octanol: water coefficient (log Kow=2.39). Field dissipation studies indicate rapid dissipation ($t_{1/2}$= 4 to 35 days) of pyroxasulfone. The presence of degradates (see **Appendix E** for structures) in the terrestrial field dissipation studies indicated that degradation was a potential route of pyroxasulfone dissipation in field studies. Leaching also was identified as a route of dissipation for the metabolite 5-difluoromethoxy-1H-pyrazol-4-yl) methanesulfonic acid (M1). This degradation product was very persistent (extrapolate $t_{1/2}$~ 8 to 65 years) in laboratory metabolism studies.

Another major degradation product (present at ≥10% applied radioactivity) was identified as 5-difluoro methoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M3). Minor degradation products (<10% of applied radioactivity) of pyroxasulfone are:

- 3-(5-Difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazole (M5),
- 3-(5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazol-4-ol (M6),
- (5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl) methanol (M8),

- 5-difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M9),
- 5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carbaldehyde (M10), and
- [3-5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-(ylmethanesulfonyl)-4,5-dihydro-5-methylisoxazol-5-yl] methanol (M11).

Additionally, there was a high percentage of applied radioactivity (8-25% of applied radioactivity) in unextracted soil/sediment residues. Because the extraction of pyroxasulfone residues was conducted using only acetonitrile/water without the use of sequentially harsher extractants, there is uncertainty regarding the identity and availability of the unextracted soil residues.

2. Overview of Pesticide Use and Usage

As a new pesticide active ingredient, the actual usage of pyroxasulfone is not known.

The registrant is proposing four product labels for pyroxasulfone including KIH-485 W85, Pyroxasulfone 85W, V10233 Herbicide Water Dispersible Granule (Commerical), and V10233 Herbicide (**Table 5**). Two products, V10233 Herbicide Water Dispersible Granule and V10233 Herbicide, are a mixture of pyroxasulfone (42.5%) and flumioxazin (33.5%). Additionally, according to the proposed labels, pyroxasulfone can be tank mixed with 2,4-D, bromacil, chlorsulfuron, dicamba, diuron, chlorpyralid, glyphosate, hexinone, imazapic, imazapyr, metsulfuron methyl, norfurazon, oryzalin, pendimethalin, picloram, pramitol, simazine, sulfometuron methyl, tebuthiuron, and triclopyr.

Table 5. Proposed Label Pyroxasulfone Use Information

Product	Crops	Application Timing	Application Method	Single Maximum Application Rate (lbs ai/A)	Maximum Seasonal Application Rate (lbs ai/A)
KIH-485 W85	Corn Soybean	Pre-plant, Pre/post-emergent, Fall application, Dry Fertilizer	Broadcast or Soil Incorporated-Ground Spray (no aerial spray applications)	0.0801 to 0.2136	0.267
Pyroxasulfone 85W	Corn, soybean, winter wheat	Pre-plant, Pre/post-emergent, Fall application, Dry Fertilizer	Broadcast or Soil Incorporated-Ground Spray (no aerial spray applications)	0.0801 to 0.2136	0.267
V-10233 Herbicide Water Dispersible Granules Commercial	Soybean Fallow land Non-Crop	Fall Burndown Spring Burndown Pre-emergent	Broadcast or Soil Incorporated-Ground Spray (no aerial spray applications)	0.062-0.093 (soy) 0.124-0.206 (non crop)	0.096 (soy) 0.206 non crop
V-10233 Herbicide	Corn Soybean Fallow Land Non-Crop		Broadcast , Band or Soil Incorporated-Ground /Aerial Spray	0.080-0.120	0.120

Two of the pyroxasulfone labels have standard runoff and ground water label advisory statements for uses on corn, soybean, fallow land, and non-crop areas. Additionally, required spray drift buffer distances are stated on theV10233 Herbicide Water Dispersible Granule (Commercial) and V10233 Herbicide labels (**Table 6**). As KIH-485 W85 and Pyroxasulfone 85W do not have required spray drift buffers, pyroxasulfone could be used on corn, soybean, and winter wheat without a spray drift buffer.

Table 6. Proposed Spray Drift Buffers

Product	Label Required Spray Drift Buffers
V-10233 Herbicide Water Dispersible Granules Commercial	Aquatic Spray Drift Buffers (ground spray): Soybean 6.5-9.8 ft Noncrop 9.8-16.4 ft Terrestrial Spray Drift Buffers (ground spray): Soybean -32 ft Non-crop-82 ft
V-10233 Herbicide	Spray Drift Buffers (aerial spray): 40 ft –non-target plants 100 ft- emerged cotton plants 40 ft – surface water (streams, wetlands, marshes, lakes, reservoirs)

The maximum single application rate of pyroxasulfone is 0.2136 lbs ai/A for corn, soybean and winter wheat with a seasonal maximum rate of 0.267 lbs ai/A (**Table 7**). Pyroxasulfone can be applied using broadcast or banded ground spray as well as aerial spray. Application timing is pre- and early post emergent. Other recommended applications include fall treatment (before ground freeze) and through dry fertilizer treatments.

Table 7. Pyroxasulfone use and application information based on the proposed label

Use	Max. Single App. Rate (lbs a.i./A)	# of App. / Season	Seasonal Max. Rate (lbs a.i./A)	Minimum App. Interval (days)
Corn, soybean, winter wheat	0.2136	1 – 2	0.267	Not specified
Corn, soybean, fallow land, non-crop	0.12	1	0.12	Not applicable
Fallow land, non-crop	0.206	1	0.206	Not applicable
Soybean	0.093	1 - 2	0.096	Not specified

C. Receptors

1. Aquatic and Terrestrial Effects

The receptor is the biological entity that is exposed to the stressor (EPA, 1998). Based on the proposed uses for pyroxasulfone, it is expected that the aquatic and terrestrial receptors will include freshwater fish and invertebrates, marine/estuarine fish and invertebrates, aquatic plants, terrestrial plants, birds, mammals, and terrestrial invertebrates.

Consistent with the process described in the Overview Document (EPA, 2004), this risk assessment uses a surrogate species approach in its evaluation of pyroxasulfone. Toxicological data generated from surrogate test species, which are intended to be representative of broad taxonomic groups, are used to extrapolate to potential effects on a variety of species (receptors) included under these taxonomic groupings.

Acute and chronic toxicity data from studies submitted by pesticide registrants are used to evaluate the potential direct effects of pyroxasulfone to the aquatic and terrestrial receptors identified in this section. This includes toxicity data on the technical grade active ingredient, any major transformation products, and when available, formulated products (e.g. "Six-Pack" studies, terrestrial plant studies).

Table 8 provides a summary of the taxonomic groups and the surrogate species tested to help understand potential acute ecological effects of pesticides to these non-target taxonomic groups. In addition, the table provides a preliminary overview of the potential acute toxicity of pyroxasulfone by providing the acute toxicity classifications.

Table 8. Test Species Evaluated for Assessing Potential Ecological Effects of Pyroxasulfone and the Associated Acute Toxicity Classification

Taxonomic Group	Surrogate Species	Acute Toxicity Classification
Birds[1]	Mallard Duck (*Anas platyrhynchos*) Bobwhite Quail (*Colinus virginianus*) Zebra finch (*Poephila guttata*)	Practically nontoxic Practically nontoxic Practically nontoxic
Mammals	Laboratory rat (Rattus norvegicus	Practically non-toxic
Insects	Honey bee (*Apis mellifera L.*)	Practically non-toxic
Freshwater fish[2]	Bluegill sunfish (*Lepomis macrochirus*) Rainbow trout (*Oncorhynchus mykiss*)	At most, moderately toxic At most, moderately toxic
Freshwater invertebrates	Water flea (*Daphnia magna*)	At most, moderately toxic
Marine/estuarine fish	Sheepshead minnow *(Cyprinodon variegatus)*	At most, moderately toxic
Marine/estuarine invertebrates	Mysid shrimp *(Americamysis bahia)* Eastern oyster (*Crassostrea virginica)*	At most, moderately toxic At most, moderately toxic
Terrestrial plants[3]	Monocots – most sensitive species Dicots – most sensitive species	No Classification
Aquatic plants and algae	Duckweed (*Lemna gibba*) Cyanobacteria/blue-green algae (*Anabaena flos-aquae*) Marine diatom (*Skeletonema costatum*) Freshwater diatom (*Navicula pelliculosa*) Algae (*Pseudokirchneriella subcapitata;* previously known as *Selenastrum capricornutum)*	No classification

[1] Birds represent surrogates for terrestrial-phase amphibians and reptiles.
[2] Freshwater fish may be surrogates for aquatic-phase amphibians.
[3] Normally four species of two families of monocots, of which one is corn; six species of at least four dicot families, of which one is soybeans.

2. Ecosystems Potentially at Risk

The ecosystems at risk are often extensive in scope, and as a result it may not be possible to identify specific ecosystems during the development of a baseline risk assessment. However, in general terms, terrestrial ecosystems potentially at risk could include the treated field and areas immediately adjacent to the treated field that may receive drift or runoff. Areas adjacent to the treated field could include cultivated fields, fencerows and hedgerows, meadows, fallow fields or grasslands, woodlands, riparian habitats, and other uncultivated areas.

Aquatic ecosystems potentially at risk might include but are not necessarily limited to water bodies adjacent to or downstream from, the treated field and might include impounded bodies such as ponds, lakes and reservoirs, or flowing waterways such as streams or rivers. For uses in coastal areas, aquatic habitat also includes marine ecosystems, including estuaries.

D. Assessment Endpoints

Assessment endpoints represent the actual environmental value that is to be protected, defined by an ecological entity (species, community, or other entity) and its attribute or characteristics (EPA, 1998). Generally, the ecological entities may include the following: freshwater as well as marine/estuarine fish and invertebrates, aquatic and terrestrial plants, birds, reptiles, amphibians, mammals, and non-target insects. The attributes for each of these entities may include growth, reproduction, and survival.

E. Conceptual Model

A conceptual model provides a written description and visual representation of the predicted relationships between pyroxasulfone residues, potential routes of exposure, and the predicted effects for the assessment endpoint. A conceptual model consists of two major components: risk hypothesis and a conceptual diagram (EPA, 1998).

1. Risk Hypothesis

For a pesticide to pose an ecological risk, it must reach ecological non-target organisms (receptors) at biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from the application site to non-target organisms. The evaluation of the ecological exposure pathways in this assessment includes an examination of the source and potential transport pathways for pyroxasulfone and the determination of exposure routes of non-target species. Based on the application methods, mode of action, fate and transport, and the sensitivity of non-target aquatic and terrestrial species, pyroxasulfone has the potential to reduce survival, reproduction, and/or growth in non-target aquatic plants (non-vascular and vascular), terrestrial plants, birds, reptiles, amphibians, and mammals when used in accordance with the proposed labels. These non-target organisms include listed and non-listed species.

2. Conceptual Diagrams

The conceptual model diagram is a generic graphic depiction of the risk hypothesis identified in the previous section. It is assumed that pyroxasulfone is capable of affecting exposed terrestrial and aquatic organisms if environmental concentrations are sufficiently elevated as a result of proposed label uses. Through a preliminary process of examining fate and effects data, the risk hypotheses and conceptual model have been refined to reflect possible exposure pathways and the organisms that are most relevant and applicable to this assessment (see figures below). If exposed at sufficient levels, mortality may occur, as well as sublethal effects. Direct effects on a taxonomic group may result in indirect effects (i.e., loss of habitat, food resources) to other taxonomic groups. This assessment will examine the potential for these effects to occur within the surrogate taxa with the intent to extrapolate to actual effects within the environment.

In order for an exposure pathway to be complete, it must have a source, a release mechanism, an environmental transport medium for pyroxasulfone and/or its transformation products, a point of exposure for ecological receptors, and a feasible route of exposure. The assessment of these pathways thus includes an examination of the sources and potential migration pathways for constituents, and the determination of potential exposure routes.

Long-range transport

Exposure to pyroxasulfone is expected to be dominated by runoff, leaching, and spray drift. Long-range transport of pyroxasulfone in the gas phase is not considered as a dominant route of exposure. Atmospheric transport is represented by dotted lines given the low likelihood of volatilization of pyroxasulfone (i.e. vapor pressure = 1.8×10^{-8} torr, MRID 47701752; and, Henry's law constant at $25^{o}C$ of 2.65×10^{-9} atm m^3/mol).

Bioaccumulation potential

This screening-level assessment for ground and aerial spray applications of pyroxsulfone considered dietary exposure (Figures 3 and 4). Log K_{ow} (2.39) is below the range (4-8) prescribed for addressing consumption of aquatic food items by piscivorous mammals and birds via KABAM v. 1.0.; this exposure route was thus eliminated from the conceptual model. Other routes of exposure that were not considered quantitatively in the assessment are incidental soil ingestion exposure and dermal exposure.

Partitioning to sediment

The partitioning properties of pyroxasulfone (K_{oc} 57-119) indicate that exposure to benthic (sediment-dwelling) invertebrates is not an exposure route of concern relative to exposure through the water column.

Dermal exposure

The dermal route of exposure for terrestrial wildlife can be divided into a few sub-routes. These include organisms exposed:

- In the treated field at the time of application or in the areas adjacent to the treated field and within the aerial drift plume that may come in direct contact with applied material.
- While conducting daily activities within treated or drift-impacted areas whereby exposure may occur via contact with dislodgeable residues of the pesticide on treated vegetation.
- To the pesticide deposited on soil particles either through contact with contaminated soil through portions of the body contacting the ground, dust bathing, or through incidental contact with fugitive dust emissions from treated or drift-impacted areas.
- Via dermal contact with the pesticide that is dissolved in puddle water on the treated field or in areas impacted by drift and run-off.
- To volatile compounds in the vapor phase integument via direct absorption.

At the present time, the Agency does not have a method to quantify these levels of exposure, and data are limited to quantify the contribution of such exposures to the toxic burden an organism experiences. The Agency is actively working on a screening method to quantify exposure from direct impingement of applied foliar sprays and from incidental contact with dislodgeable foliar pesticide residues from treated or drift-impacted vegetation.

Inhalation exposure

The Screening Tool for Inhalation Risk (STIR v.1.0, November 19, 2010) was used to calculate an upper bound estimate of exposure using pyroxasulfone's vapor pressure (1.8 x 10^{-8} torr) and molecular weight (367 g/mol) for vapor phase exposure as well as the maximum application rate and method of application for spray drift. STIR incorporates results from several toxicity studies including acute oral and inhalation rat toxicity endpoints obtained from the "six-pack" of core studies, which are a series of six guideline studies that are submitted to the Registration Division of the Office of Pesticide Programs for technical and formulated products of a pesticide (acute oral LD_{50} >2000 mg a.i./kg-bw, MRID 47701677; and, acute inhalation LC_{50} > 6.56 mg a.i./L, a test duration of 4.5 hours MRID 47701685) as well as the most sensitive acute oral avian toxicity endpoint (acute oral LD_{50}>2250 mg a.i./kg-bw for the northern bobwhite quail, MRID 47701631). Based on the results of the STIR model, inhalation exposure alone not determined to be a potential pathway of concern for both avian and mammalian species on an acute basis.

Inhalation exposure via spray drift and vapor-phase of the pesticide alone does not appear to be of concern. The maximum seasonal and single rates were used in the tool for ground spray (0.267 and 0.2136 lbs a.i./A, respectively) and aerial spray (0.120 lbs a.i./A) applications; all yielded the same result (see **Appendix A** for a sample result). The analysis of the inhalation route in STIR does not consider that aggregation with other

exposure pathways such as dietary, dermal, or drinking water may contribute to a total exposure that has a potential for effects to non-target animals. However, the Agency does consider the relative importance of other routes of exposure in situations where data indicate that pesticide exposures through other routes may be potentially significant contributors to wildlife risk (USEPA, 2004). The risk characterization section, discusses the impact of consideration of other routes of exposure, particularly ingestion, that have been identified as potentially important and the degree of certainty associated with screening-level risk assessment conclusions. Detailed information about STIR v.1.0, as well as the tool, can be found on the EPA's website at:
http://www.epa.gov/pesticides/science/models_pg.htm#terrestrial.

Drinking water exposure

Drinking water for the purposes of terrestrial organism risk assessment is defined as that portion of an organism's daily water intake that is not met by dietary or metabolic sources and must be consumed in liquid form. Typical drinking water sources for wildlife in pesticide use areas may include on-field puddles, irrigation equipment (e.g., drip irrigation in grape cultivation), dew deposited on treated plants, and off-field surface water exposures.

The Screening Imbibition Program (SIP v.1.0, Released June 15, 2010) was used to calculate an upper bound estimate of exposure using pyroxasulfone's solubility (3.49 mg/L at 25°C), the most sensitive acute (LD_{50}>2250 mg a.i./kg-bw for the northern bobwhite quail, MRID 47701631) and chronic (NOAEC of 60 mg a.i./kg-diet for the mallard duck, MRID 47701636) avian toxicity endpoints and the most sensitive acute (LD_{50} > 2000 mg a.i./kg-bw for the rat, MRID 47701677) and chronic (NOAEL of 7.2 mg/kg-bw/day for the rat, MRID 47701706) mammalian toxicity endpoints. Drinking water exposure alone was not determined to be a potential pathway of concern for either avian or mammalian species on either an acute or chronic basis (see **Appendix B**).

Although drinking water exposure alone does not appear to be of concern, this does not take into account that when aggregated with other exposure pathways (dietary food sources, dermal, inhalation) drinking water may contribute to a total exposure that has a potential for effects on non-target animals and should be explored further. Because there is a high degree of conservatism in the SIP 1.0 exposure estimate, there is limited expectation that use scenarios not triggering a SIP 1.0 concern would contribute significantly to aggregate risks from water plus diet when a refined water exposure model is incorporated in the actual quantitative risk assessment. Detailed information about SIP v.1.0, as well as the tool, can be found on the EPA's website at
http://www.epa.gov/pesticides/science/models_pg.htm#terrestrial.

Figure 3. Conceptual model depicting stressors, exposure pathways, and potential effects to aquatic organisms from pyroxasulfone use on corn, soybeans, wheat, fallow land, and non-crop areas. Dotted lines indicate exposure pathways that have a low likelihood of contributing to ecological risk.

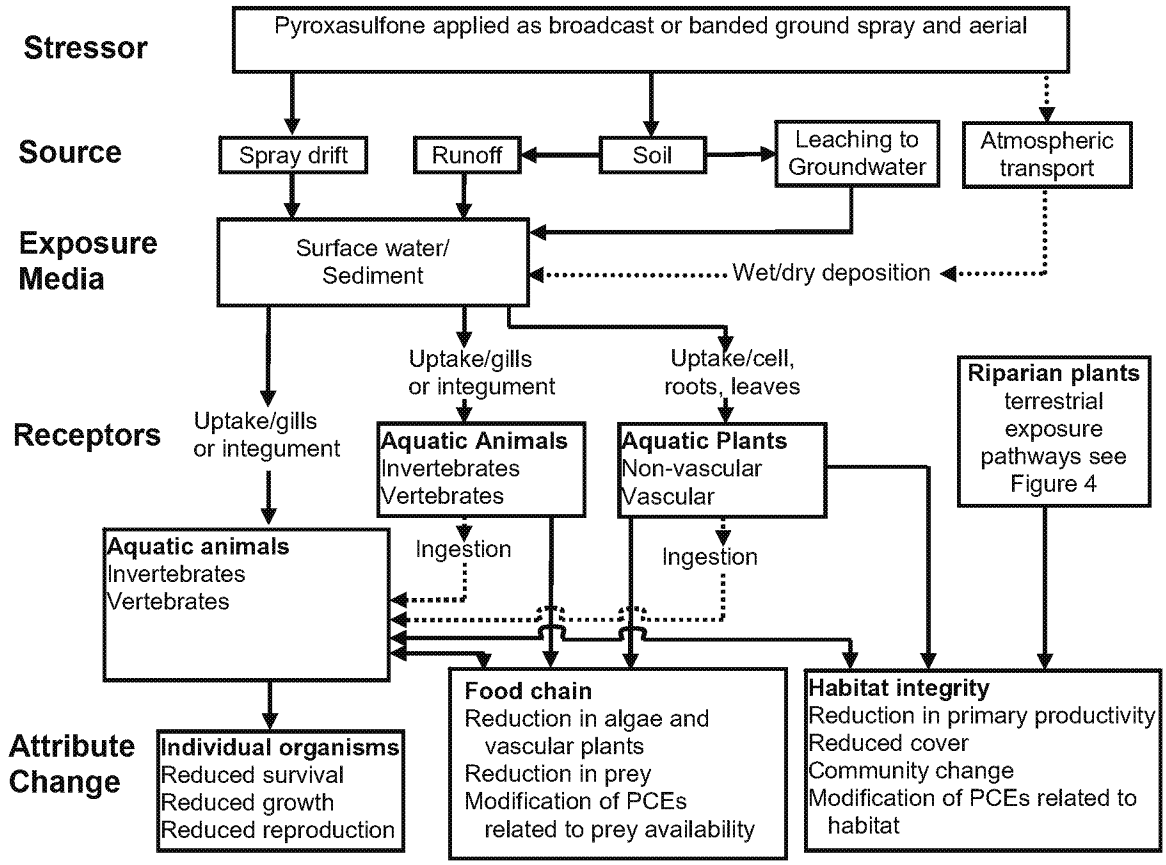
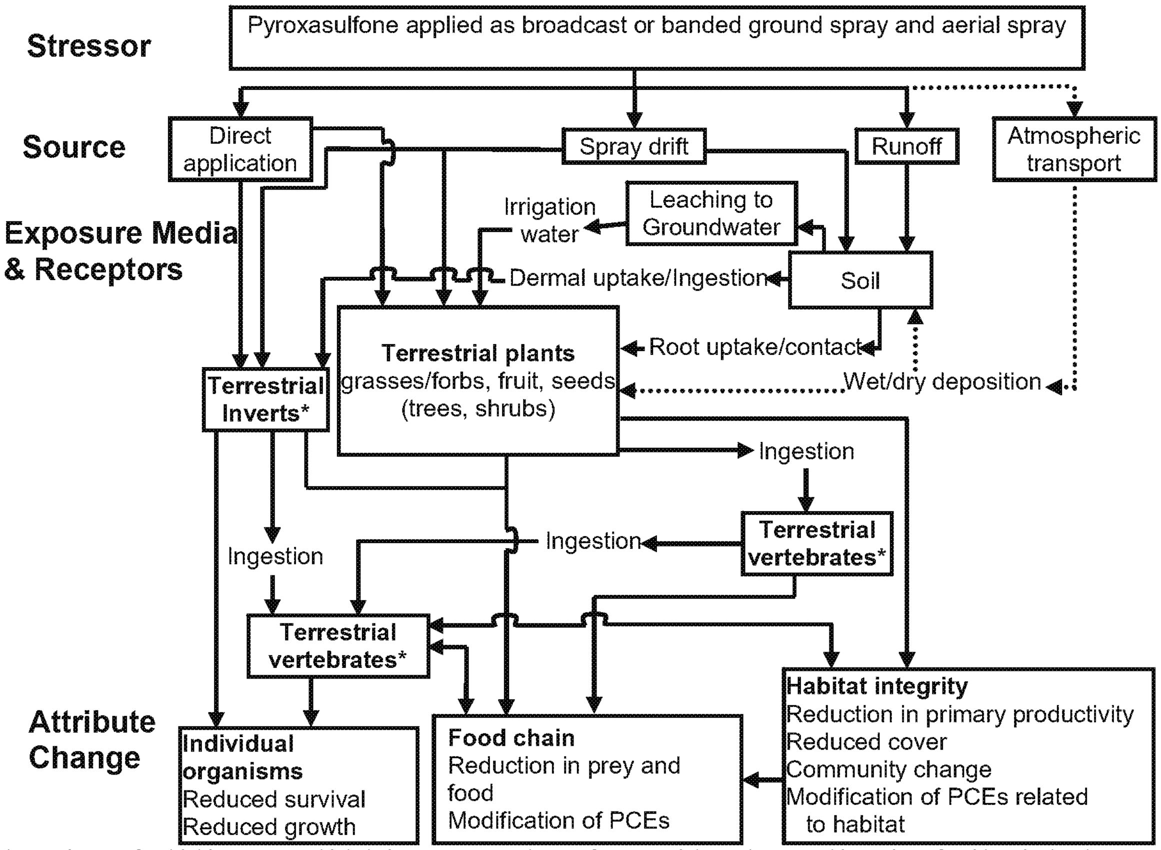
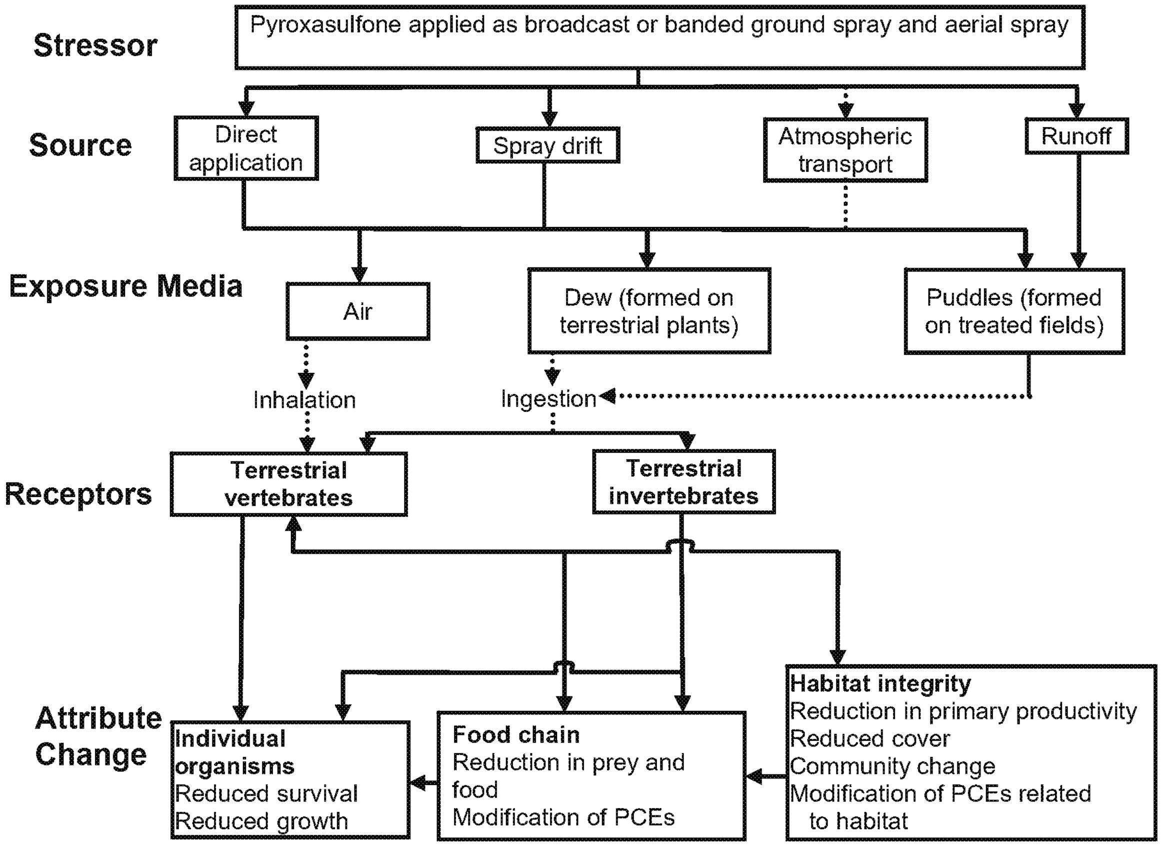


Figure 4. Conceptual model depicting stressors, generic exposure pathways, and potential effects to terrestrial organisms from pyroxasulfone use on corn, soybeans, wheat, fallow land, and non-crop areas. Dotted lines indicate exposure pathways that have a low likelihood of contributing to ecological risk.



* See Figure 5 for drinking water and inhalation exposure pathways for terrestrial vertebrates and ingestion of residues in dew by terrestrial invertebrates

Figure 5. Conceptual model depicting stressors, drinking water and inhalation exposure pathways, and potential effects to terrestrial animals from use of pyroxasulfone on corn, soybeans, wheat, fallow land, and non-crop areas. Dotted lines indicate exposure pathways that have a low likelihood of contributing to ecological risk.



F. Analysis Plan

The structure of this risk assessment is based on guidance contained in U.S. EPA's *Guidance for Ecological Risk Assessment* (U.S. EPA, 1998) and is consistent with procedures and methodology outlined in the Overview Document (U.S. EPA, 2004).

1. Conclusions from Previous Risk Assessments

There are no previous Agency ecological risk assessments because this is the first registration petition for pyroxasulfone for use on field corn, popcorn, sweet corn, soybeans, winter wheat, fallow land, non-crop areas around farms, orchards and vineyards and to maintain bare ground on non-crop areas in the United States.

2. Preliminary Identification of Data Gaps

Review of the submitted studies indicated the following points:

Environmental Fate
The submitted fate database is incomplete for pyroxasulfone on account of the need for ground water monitoring data. In addition, an uncertainty in the environmental fate data is the identification and availability of unextracted residues in soil and aquatic metabolism studies. These residues account for a high percentage of applied radioactivity (8-25% of applied radioactivity). Although there is an uncertainty regarding the identification and quantification of unextracted soil/sediment residues, this uncertainty does not substantially affect the estimated exposure levels due to the persistence of pyroxasulfone. For a list of submitted environmental fate studies for pyroxasulfone, see Section V.

Data needs:
Because pyroxasulfone is mobile and persistent in soil it has the potential to leach into groundwater. This behavior was predicted using Tier II PRZM GW model. This modeling showed that pyroxasulfone has the potential to accumulate in groundwater.

- Prospective ground water monitoring study.

Ecotoxicity
The submitted ecotoxicity database is incomplete. For a list of submitted ecological effects studies for pyroxasulfone see Section V. The following studies are considered data gaps:

<u>Chronic Marine/Estuarine Fish Study</u>
No chronic studies on marine/estuarine fish were submitted by the registrant. Therefore, a quantitative estimation of risk could not be conducted. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is stable to hydrolysis (at pHs 4, 7, and 9) and aqueous photolysis (half life = 119 days), comparison to freshwater fish data suggests that chronic risk to marine/estuarine fish is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean wheat, and non-crop sites. Therefore, a chronic marine/estuarine fish study is not required.

- Chronic: Fish early-life stage (saltwater: *Cyprinodon variegatus*) (850.1400; 72-4), TGAI

<u>Chronic Marine/Estuarine Invertebrate Study</u>
No chronic studies on marine/estuarine invertebrates were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is stable to hydrolysis (at pHs 4, 7, and 9) and aqueous photolysis (half life = 119 days), comparison to freshwater invertebrate data suggests that chronic risk to marine/estuarine invertebrates is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean,

wheat, and non-crop sites. Therefore, a chronic marine/estuarine invertebrate study is not required.

- Chronic: Marine/estuarine invertebrate (*Americamysis bahia*) (850.1350; 72-4), TGAI

Fish Bioaccumulation Study

A bioaccumulation in fish study was not submitted to support the proposed registration. According to CFR 40 Part 158, this data is conditionally required and although pyroxasulfone is mobile and persistent, the low octanal:water partitioning coefficient (log K_{ow}= 2.39) is expected to limit bioconcentration and bioaccumulation of pyroxasulfone. Based on the log K_{ow} of 2.39, the expected BCF assuming no metabolism and 5% lipids would be approximately 12 L/kg wet weight (*i.e.,* $10^{2.39} * 0.05$). This low BCF combined with the low acute toxicity to birds and mammals indicates that risks to piscivorous wildlife would not be expected. Therefore, a fish bioaccumulation study is not required.

- Fish Bioaccumulation study (850.1730; 72-6, 165-4), TGAI

3. Measures of Exposure and Effects

EFED uses a tiered system of pesticide exposure modeling to assess ecological risk following a registered application of that pesticide. This tiered system is designed to minimize the amount of analysis which is required to register any given chemical. Each of the tiers is designed to screen out pesticides by requiring higher, more complex levels of investigation only for those that have not passed the next lower tier. Each tier screens out a percentage of pesticides from having to undergo a more rigorous review prior to registration or re-evaluation.

a. Aquatic Exposure Models

Tier II PRZM and EXAMS[2] simulation models were used to estimate the exposure concentrations of pyroxasulfone in surface water for the proposed use on corn, soybean, wheat, and noncrop areas. The results are presented in **Appendix C**. The data used as input parameters come solely from the environmental fate studies and proposed product labels submitted by the petitioner to support the United States registration of pyroxasulfone.

[2] PRZM 3.1.2.2 (5/16/05) and EXAMS 2.98.04(4/25/04) were used rather than GENEEC2 (4/25/04) in anticipation of toxicity concerns for aquatic organisms.

b. Terrestrial Exposure Models

T-REX Model

The focus of terrestrial wildlife exposure estimates is for birds (also acting as surrogate for reptiles and terrestrial-phase amphibians) and mammals with an exposure route emphasis on uptake through the diet. The residues in or on potential dietary sources for mammals and birds (e.g., vegetation, insects, and seeds) were estimated using the Tier I model T-REX (Version 1.4.1, 2008). In this Tier I assessment, it was assumed that organisms are exposed to one active ingredient in a given exposure scenario. In all screening-level assessments, the organisms are assumed to consume 100% of their diet as one food type and one food source. The T-REX output is presented in the Risk Characterization section of this document as well as an example in **Appendix D**.

The approach used to estimate exposure of terrestrial animals to pyroxasulfone was based on potential foliar applications of pyroxasulfone. Upper-bound exposure levels were calculated for spray applications of proxasulfone using maximum proposed application rates for one application for the proposed uses. The exposure estimates are based on a database of pesticide residues on wildlife food sources associated with specified application rates (Kenaga, 1972; Fletcher et al., 1994). Essentially, for a single application, there is a linear relationship between the amount of pesticide applied and the amount of pesticide residue present on a given food item. Food item residue levels are then linearly adjusted based on application rate. The upper-bound estimates are used to estimate risks since these values represent the high-end exposure that may be encountered for terrestrial species that consume food items that have received label-specified pesticide application. Although these represent higher-end estimates, they do not represent the highest possible exposure estimates. With regard to bare ground applications, T-REX EECs account for residue values on potential dietary items (terrestrial invertebrates and/or plants) found immediately adjacent to or on the treated field. These assumptions are relevant for labels that include non-crop uses for this particular chemical, including V-10233 Herbicide and the water dispersible granule version. However, these labels are multi-active ingredient products (*i.e.*, containing 42.2% pyroxasulfone and 33.6 flumioxazin), the mixture of which is not accounted for by TREX. Instead, the model calculates EECs on a single active ingredient (*i.e.*, pyroxasulfone only) basis.

T-REX is a simulation model that, in addition to incorporating the relationship between application rate and food item residue concentrations, accounts for pesticide degradation in the estimation of terrestrial EECs. T-REX calculates pesticide residues on each type of food item on a daily interval for one year. A first-order decay function is used to calculate the residue concentration at each day based on the concentrations present from both initial and all subsequent applications. The decay rate is dependent on the foliar dissipation half-life. The food item concentration on any given day is the sum of all residues up to that day, taking into account the first-order degradation. The initial application occurs on day 0 (t=0) and the model runs for 365 days. Over the 365-day run, the highest residue concentration is the measure of exposure (EEC) used to calculate risk quotients (RQs).

The foliar dissipation half-life and residue decline studies can be important in estimating exposure because they essentially determine how long the pesticide remains in or on food items after application. In many cases, neither empirically determined foliar dissipation nor residue decline half-life (with a day 0 residue) values are available, in which case the default value of 35 days is used (Willis and McDowell, 1987). That was the case for this assessment. The maximum *seasonal* application rate was used to calculate RQs given that the maximum single application rates were either equal or approximately equal to the seasonal rate. In addition, given that application intervals were not reported on the labels and pyroxasulfone's persistence in water (half-lives ranging from 69 to 119 days) and soil (half-lives ranging from 142 to 533 days), the maximum *seasonal* rate was assumed appropriate for RQ calculations. Furthermore, the seasonal application rate was assumed to be equivalent to annual application rate.

In cases where RQs exceeded LOCs at the maximum *seasonal* rate, two applications (that totaled the maximum seasonal rate) were modeled and used for risk characterization. T-REX does not currently allow for variable application rates/applications or different application intervals between applications. Therefore, to account for the variable application rates described on the proposed labels for corn, soybean, and winter wheat, the EECs for the different potential food items were estimated by summing the 3-day EEC for the initial application (0.2136 lbs a.i./A) with the peak EEC value (day 0) for the subsequent application (0.0534 lbs a.i./A). The summed EECs were calculated in this manner for each food type and the values were used as a basis for generating equivalent dietary-based EECs in T-REX to calculate RQ values (Table 32).

TERRPLANT Model

The TerrPlant (Ver.1.2.2) model is used to predict EECs from terrestrial uses for terrestrial plants located in dry and semi-aquatic areas adjacent to the treated field or treated water body. A semi-aquatic area is defined as a low-lying area of terrestrial habitat that is wet but may dry up at times throughout the year. TerrPlant incorporates two similar conceptual models for depicting dry and semi-aquatic areas of terrestrial habitats. For both models, a non-target area is adjacent to the target area. Pesticide exposures to plants in the non-target area are estimated to receive runoff and spray drift from the target area.

For a dry area adjacent to the treatment area, runoff exposure is estimated as sheet runoff. Sheet runoff is the amount of pesticide in water that runs off of the soil surface of a target area of land which is equal in size to the non-target area (1:1 ratio of areas). In the sheet runoff scenario, the treated area generating runoff is assumed to drain into an area with equal size containing seedlings, resulting in 1, 2, or 5% of the application rate being deposited. For semi-aquatic areas, runoff exposure is estimated as channel runoff.

Channel runoff is the amount of pesticide that runs off of a target area 10 times the size of the non-target area (10:1 ratio of areas). In the channel runoff scenario, a ten-to-one ratio of watershed area to receiving area results in 10, 20, or 50% of the application rate being deposited on soil with emerging or emerged seedlings. The magnitude of runoff is assumed to be dependent on the water solubility of the pesticide active ingredient. For pesticides with a solubility of <10, 10 to 100, or >100 ppm, runoff fractions of 0.01, 0.02 or 0.05 respectively are selected by the model user.

Exposures through runoff and spray drift are then compared to measures of survival and growth (e.g. effects to seedling emergence and vegetative vigor) to develop RQ values. The model compares the combined deposition estimates from runoff and spray drift to adverse effect levels measured in seedling emergence studies. In addition, RQs are derived for plants with consideration for spray drift exposures. For monocots and for dicots, TerrPlant compares estimated spray drift deposition, without a runoff exposure component, to the more sensitive measure of effect, either seedling emergence or vegetative vigor (USEPA 2005).

Not unlike the modeling in T-REX, the maximum *seasonal* application rate was used to calculate RQs given that the maximum single application rates were either equal or approximately equal to the seasonal rate. In addition, given that application intervals were not reported on the labels and pyroxasulfone's persistence in water (half-lives ranging from 69 to 119 days) and soil (half-lives ranging from 142 to 533 days), the maximum *seasonal* rate was assumed appropriate for RQ calculations. Nevertheless, in cases where RQs exceeded LOCs, lower application rates were used for risk characterization. Furthermore, the seasonal application rate was assumed to be equivalent to annual application rate.

Irrigation Model

Because pyroxasulfone is a mobile and persistent herbicide, there is potential for terrestrial plant effects from exposure through irrigation water. Although this is not a standard modeling approach in OPP, it is being implemented for incorporation into ecological risk assessments for pesticides with phytotoxic effects.

To estimate exposure to plants when groundwater contaminated by pyroxsulfone is applied to crops, the following method was used. It is assumed a one-acre field is irrigated with one inch of water containing pyroxsulfone. Pyroxsulfone concentrations were estimated using beta version of the PRZM GW Tier II model. This model is currently undergoing an implementation process in OPP. The model provides ground concentration as predicted through the Pesticide Root Zone Model (PRZM).

Table 9 summarizes the measures of ecological effects and exposure used to assess ecological risk following exposure to pyroxasulfone with the proposed uses.

Table 9. Measures of Ecological Effects and Exposure for Pyroxasulfone			
Assessment Endpoint		**Surrogate Species and Measures of Ecological Effect[1,2]**	**Measures of Exposure**
Birds[3]	Survival	Bobwhite Quail acute oral LD_{50}, subacute dietary LC_{50} Mallard Duck subacute dietary LC_{50} Zebra Finch acute oral LD_{50}	Upper bound residues on food items (foliar)
	Reproduction and growth	Bobwhite Quail reproduction NOAEC/LOAEC Mallard Duck reproduction NOAEC/LOAEC	
Mammals	Survival	Laboratory rat acute oral LD_{50}	
	Reproduction and growth	Laboratory rat reproduction and development NOAEL/LOAEL Rabbit development NOAEL/LOAEL	
Freshwater fish[4]	Survival	Rainbow trout 96-hr LC_{50} Bluegill sunfish 96-hr LC_{50}	Peak EEC[5]
	Reproduction and growth	Fathead minnow NOAEC/LOAEC	60-day average EEC[5]
Freshwater invertebrates	Survival	Water flea 48-hr EC_{50}	Peak EEC[5]
	Reproduction and growth	Water flea NOAEC/LOAEC	21-day average EEC[5]
Marine/estuarine fish	Survival	Sheepshead minnow 96-hr LC_{50}	Peak EEC[5]
	Reproduction and growth	No study available	60-day average EEC[5]
Marine/estuarine invertebrates	Survival	Eastern oyster 96-hr EC_{50} Saltwater mysid 96-hr LC_{50}	Peak EEC[5]
	Reproduction and growth	Saltwater mysid NOAEC/LOAEC	21-day average EEC[5]
Terrestrial plants[6]	Survival and growth	Monocot Seedling emergence EC_{25}, NOAEC or EC_{05} Monocot Vegetative Vigor EC_{25}, NOAEC or EC_{05} Dicot Seedling emergence EC_{25}, NOAEC or EC_{05} Dicot Vegetative Vigor EC_{25}, NOAEC or EC_{05}	Estimates of runoff and spray drift to non-target areas
Terrestrial invertebrates	Survival	Honey bee acute contact 48-hr LD_{50}, Parasitoid wasp & predatory mite ER_{50}/LR_{50}, Earthworm 14-day LC_{50}, 28-day NOAEC	Maximum application rate
Aquatic plants and algae	Survival and growth	Duckweed 7-day EC_{50}, NOAEC Freshwater green algae 96-hr EC_{50}, NOAEC Freshwater blue-green algae 96-hr EC_{50}, NOAEC Freshwater diatom 96-hr EC_{50}, NOAEC Marine diatom 96-hr EC_{50}, NOAEC	Peak EEC[5]

[1] LD_{50} = Lethal dose to 50% of the test population; NOAEC = No observed adverse effect concentration; LOAEC = Lowest observed adverse effect concentration; LC_{50} = Lethal concentration to 50% of the test population; EC_{50}/EC_{25} = Effect concentration to 50%/25% of the test population.
[2] Species listed in this table represent the most commonly encountered species from registrant-submitted studies, risk assessment guidance indicates the most sensitive species tested within each taxonomic group are to be used for baseline risk assessments.
[3] Birds represent surrogates for amphibians (terrestrial phase) and reptiles.
[4] Freshwater fish may be surrogates for amphibians (aquatic phase).
[5] One in 10-year return frequency.
[6] Four species of two families of monocots - one is corn, six species of at least four dicot families, of which one is soybeans.

III. Analysis

A. Use Characterization

Pyroxasulfone is a new herbicide in the pyrazole class; also considered an oxazole, K-3 herbicide, and a sulfonylioxazoline (acetolactase synthase, ALS inhibitor). What is known is that the chemical inhibits biosynthesis of very-long-chain fatty acids (VLCFAs) - that are contained in the plasma membrane of plant cells - by preventing fatty acid precursors (medium- and long-chain fatty acids, which are formed in the chloroplast) from elongating into chains (in the endoplasmic reticulum). Ultimately, this effect leads to inhibition of plant shoot growth. Weedy species such as barnyard millet and Italian ryegrass, but also rice were determined to be sensitive to pyroxasulfone; wheat and corn to a lesser degree (Shimizu *et al.* 2009 MRID 47701754). It is unclear at this time to what degree the mechanism of VLCFA formation in animal cells might be affected as a result of exposure to pyroxasulfone.

The maximum single application rate of pyroxasulfone is 0.2136 lbs ai/A with a seasonal maximum rate of 0.267 lbs ai/A. Pyroxasulfone can be applied using broadcast or banded ground spray as well as aerial spray. Application timing is pre- and early post emergent. Other recommended applications include fall treatment (before ground freeze) and through dry fertilizer treatments. Depending on the crop, the recommended crop rotation intervals range 4 to 12 months. At this time pyroxasulfone use is proposed only on certain major crops (corn, soybeans, and wheat); there is an expansive exposure potential to pyroxasulfone and its degradation products with these crop uses.

B. Exposure Characterization

1. Environmental Fate and Transport

Summary

Pyroxasulfone is mobile (K_{oc}= 57-119 L/kg) and persistent ($t_{1/2}$= 142 to 533 days) in terrestrial and aquatic environments (Table 3). The major routes of dissipation are expected to be associated with microbial-mediated degradation, leaching, and runoff. Pyroxasulfone is stable to hydrolysis and photodegradation in water and soil. Volatility is not expected to be a major dissipation pathway because of the low vapor pressure ($1.8E^{-8}$ torr) and Henry's Constant ($2.65E^{-9}$ atm-m3/mole). Also, the bioaccumulation potential of pyroxasulfone is expected to be low due to a low octanol: water coefficient (log Kow=2.39). Field dissipation studies indicate rapid dissipation ($t_{1/2}$= 4 to 35 days) of pyroxasulfone. The presence of degradates (see **Appendix E** for structures) in the terrestrial field dissipation studies indicated that degradation was a potential route of pyroxasulfone dissipation in field studies. Leaching also was identified as a route of dissipation for the metabolite 5-difluoromethoxy-1H-pyrazol-4-yl) methanesulfonic acid (M1). This degradation product was very persistent (extrapolate $t_{1/2}$~ 8 to 65 years) in laboratory metabolism studies.

Another major degradation product (present at ≥10% applied radioactivity) was identified as 5-difluoro methoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M3). Minor degradation products (<10% of applied radioactivity) of pyroxasulfone are:

- 3-(5-Difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazole (M5),
- 3-(5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazol-4-ol (M6),
- (5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl) methanol (M8),
- 5-difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M9),
- 5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carbaldehyde (M10), and
- [3-5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-(ylmethanesulfonyl)-4,5-dihydro-5-methylisoxazol-5-yl] methanol (M11).

Additionally, there was a high percentage of applied radioactivity (8-25% of applied radioactivity) in unextracted soil/sediment residues. Because the extraction of pyroxasulfone residues was conducted using only acetonitrile/water without the use of sequentially harsher extractants, there is uncertainty regarding the identity and availability of the unextracted soil residues.

In Tier II PRZM/EXAMS modeling the post-plant application of pyroxasulfone in the MS corn scenario produced the highest estimated exposure concentrations (EECs). The maximum 1 in 10 year for pyroxasulfone was 8.341 µg/L for daily peak EEC, 8.137 µg/L for 21-day average EEC, and 7.779 µg/L for 60-day average EEC. Degradation products were not considered in the exposure modeling because of the persistence of pyroxasulfone. In addition, surface water modeling for total residues (parent+M1+M3) showed a small difference in exposure concentrations when compared with modeling for the parent.

Persistence

Pyroxasulfone was stable to abiotic hydrolysis in pH 5, 7, and 9 buffer solutions (MRID 47701733). It was also essentially stable to photodegradation in water and soil (MRID 47701734 and 47701735). The photodegradation half-life in water was 119 days. Pyroxasulfone was persistent in aerobic soil with half-lives ranging from 142 to 533 days across ten soils (MRID 47701737 and 47701736). The mean aerobic soil metabolism half-life was 343.8 days (N=10) with a standard deviation of 119.9 days. In two anaerobic soils, pyroxasulfone half-lives range from 145 to 156 days (MRID 47701739). Pyroxasulfone was moderately persistent in aerobic and anaerobic aquatic environments (MRID 47701741and 47701740). The mean total sediment and aquatic half-life was 108.5days (SD= 0.7 days; N=2) and 70.25 days (SD=0.8 days; N=2) in aerobic aquatic environments and anaerobic aquatic environments, respectively.

Degradation Products

Metabolite identification was conducted on acetonitrile/water (2:1 v:v) extractable residues from water, soil, and sediment. Major metabolites (≥10% of applied radioactivity) of pyroxasulfone in laboratory metabolism studies were 5-difluoromethoxy-1H-pyrazol-4-yl) methanesulfonic acid (M1) and 5-difluoro methoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4- carboxylic acid (M3).

Minor metabolites (<10% of applied radioactivity) were 3-(5-Difluoromethoxy-3-trifluoromehyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazole (M5), 3-(5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl methanesulfonyl)-4,5-dihydro-5,5-dimethylisoxazol-4-ol (M6), (5-difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl) methanol (M8), 5-difluoromethoxy-3-trifluoromethyl-1H-pyrazol-4-carboxylic acid (M9), 5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-carbaldehyde (M10), and [3-5-Difluoromethoxy-1-methyl-3-trifluoromethyl-1H-pyrazol-4-ylmethanesulfonyl)-4,5-dihydro-5-methylisoxazol-5-yl] methanol (M11). Unidentified residues in metabolism studies accounted for 1.2 to 3.3% of applied radioactivity. Bound soil/sediment residues (post acetonitrile/water extraction) account for 8 to 25% of the applied radioactivity.

Table 10 shows the maximum concentration of each degradation product in each laboratory environmental fate study.

Table 10. Degradation Product Identification in Laboratory Studies

Degradation Product	Study	Max% Applied Radioactivity (day)	MRID
KIH-485 M1	Aerobic Soil Metabolism	49 (365d)	47701736
		42.3 (181d)	47701737
		1.2 (180d)	
		27.5 (365d)	
		1.6 (365 d)	
		27.6 (365d)	
		1.0 (120d)	
		35.9 (365d)	
		1.0 (181d)	
	Aerobic Aquatic Metabolism	16.1 (180 d)	47701740
		0.6 (180 d)	
	Anaerobic Aquatic Metabolism	20.6 (365 d)	47701741
KIH-485 M3	Aerobic Soil Metabolism	7.1 (90d)	47701736
		3.4 (90 d)	47701737
		2.3 (120 d)	
		6.8 (181 d)	
		10.3 (365d)	
		7.1 (90d)	
	Aerobic Aquatic Metabolism	12.8 (180 d)	47701740

	Anaerobic Aquatic Metabolism	6.5 (181 d)	47701741
KIH-485 M5	Soil Photolysis	0.3 (30d)	47701735
KIH-485 M6	Aerobic Soil Metabolism	2.3(90d)	47701736
		2.2(90d)	47701737
		1.4 (365 d)	
		0.6 (182 d)	
		1.0 (181d)	
	Anaerobic Soil Metabolism	1.5 (61 d)	47701739
	Soil Photolysis	0.5 (21 d)	47701735
	Aerobic Aquatic Metabolism	0.9 (61d)	47701740
KIH-485 M8	Anaerobic Soil Metabolism	3.7 (303 d)	47701739
	Aerobic Aquatic Metabolism	3.8 (29 d)	47701740
	Anaerobic Aquatic Metabolism	6.4 (120d)	47701741
KIH-485 M9	Aerobic Soil Metabolism	1.8(90d)	47701736
	Anaerobic Soil Metabolism	1.4 (30 d)	47701739
	Aerobic Aquatic Metabolism	6.2 (120 d)	47701740
	Anaerobic Aquatic Metabolism	2.1 (120 d)	47701741
KIH-485 M10	Anaerobic Soil Metabolism	6.2 (180 d)	47701739
	Aerobic Aquatic Metabolism	0.6 (61 d)	47701740
	Anaerobic Aquatic Metabolism	7.8 (365d)	47701741
KIH-485 M11	Aerobic Aquatic Metabolism	0.5 (61 d)	47701740
		1.2 (180 d)	
KIH-485 M13	Aerobic Aquatic Metabolism	1.9 (180 d)	47701740
		2.9 (180 d)	
	Anaerobic Aquatic Metabolism	2 (181 d)	47701741

Mobility

Pyroxasulfone and its degradation products M1, M3, and M6 were highly mobile to mobile in four soil and aquatic environments (MRID 47701742, 47701743, 47701744). The Freundlich adsorption coefficient for pyroxasulfone was 1.93 L/kg (1/n=1; K_{oc}=104) in sandy clay loam, 1.93 L/kg (1/n=0.9880; K_{oc}=99) in clay loam, 1.59 L/kg (1/n=0.9898; K_{oc}=119), and 2.00 L/kg (1/n=1; K_{oc}=57) in loam. The Freundlich desorption coefficient was 4.10 L/kg (1/n=0.9590; K_{oc}=216) in sandy clay loam, 7.44 L/kg (1/n=0.9289; K_{oc}=169) in clay loam, 3.16 L/kg (1/n=0.9208; K_{oc}=226), and 4.16 L/kg (1/n=0.9650; K_{oc}=119) in loam. Pyroxasulfone was leached through packed soil columns; 42.5 to 90.3% of applied radioactivity was detected in the soil column leachate. The radioactivity in leachate samples were identified as pyroxasulfone (72.6 to 84% of applied dose), M1 (7.5 to 18.6% of applied dose), M3 (2.6 to 4.2% of applied dose), and M6 (1.1 to 6.7% of applied dose). The column K_d for pyroxasulfone was 1.19 mL/g in IL silt loam soil, 1.10 mL/g in GA sandy loam soil, 0.635 mL/g in CA silt loam soil and 1.98 mL/g in NY clay loam. The soil column K_d for M1 is 0.754 mL/g in IL silt loam soil, 0.620 mL/g in GA sandy loam soil, 0.568 mL/g in CA silt loam soil and 0.816 mL/g in NY clay loam.

Field Dissipation Studies

Pyroxasulfone (formulated as KIH-485 WG85) was broadcast spray applied at 67.2 g ai/A (0.15 lbs ai/A) in CA, 84.6 (0.19 lbs ai/A) in IL and GA, and 121.4 g ai/A (0.27 lbs ai/A) in NY (MRID 47701745). The dissipation DT50 for pyroxasulfone in surface soil (0-15 cm) was 35 days in CA, 16.7 days in IL, 24 days in GA, and 4 days in NY. Pyroxasulfone was predominately detected in the surface soil (0-15 cm). There were sporadic detections of pyroxasulfone with soil depth at the CA and GA site. Pyroxasulfone residue leaching was determined in 6 inch soil samples to a soil depth of 36 inches. The maximum depth of pyroxasulfone leaching was 12 to 18 inches (0.011 mg/kg) at the CA site and 12 to 18 inches (0.007 mg/kg) at the GA site. The degradation product M3 was detected at concentration of 0.006 mg/kg in the 12 month after treatment (MAT) surface soil (0-6 inches) at the CA site, 0.003 mg/kg in the 1 month after treatment (MAT) surface soil (0-6 inches) at the NY site, and 0.003 mg/kg in the 14 days after treatment (DAT) surface soil (0-6 inches) at the IL site. The degradation product M1 was detected at concentration of 0.006 mg/kg in the 10 month after treatment (MAT) surface soil (0-6 inches) at the CA site, 0.013 mg/kg in the 1 MAT surface soil (0-6 inches) at the NY site, 0.011 mg/kg in the 14 DAT surface soil (0-6 inches) at the GA site. There were detections of M1with depth at the IL (6-12 inches at 0.004 mg/kg) and GA (18-24 inches at 0.005 mg/kg).

Pyroxasulfone (formulated as KIH-485 WG85P) was broadcast spray applied at 121.4 g ai/A (0.27 lbs ai/A) at CA and AR field sites (MRID 47701747). The sites were flooded immediately after pyroxasulfone application and then drained after 130 to152 days after application. Samples were taken to represent sediment, flood water, and soil after flooding. The dissipation DT50 for pyroxasulfone in surface sediment (0-6 inches) was

77 days in CA and 64.8 days in AR. The dissipation DT50 for pyroxasulfone in water was 16 days at both sites. Pyroxasulfone was the only residue in flood water. M1 and M3 were not detected in the flood water. Pyroxasulfone, M1, and M3 were not detected in post flood soils (0-18 inches).

Bioaccumulation in Fish

A bioaccumulation in fish study was not submitted to support the proposed registration. Although the pyroxasulfone is mobile and persistent, the low octanal:water partitioning coefficient (log K_{ow}= 2.39) is expected to limit bioconcentration and bioaccumulation of pyroxasulfone. Based on the log K_{ow} of 2.39, the expected BCF assuming no metabolism and 5% lipids would be approximately 12 L/kg wet weight (*i.e.,* $10^{2.39} * 0.05$). This low BCF combined with the low acute toxicity to birds and mammals indicates that risks to piscivorous wildlife would not be expected.

2. Measures of Aquatic Exposure

a. Aquatic Exposure Modeling

The estimated environmental concentrations (EECs) reported in the assessment were calculated using the Tier II model for surface water (PRZM/EXAMS). Sample inputs and outputs of the model are presented in **Appendix C**.

PRZM (v3.12.2, May 2005) and EXAMS (v2.98.4.6, April 2005) are screening simulation models coupled with the input shell pe5.pl (Aug 2007) to generate daily exposures and 1-in-10 year EECs of pyroxasulfone that may occur in surface water bodies adjacent to application sites receiving pyroxasulfone through runoff and spray drift for specific scenarios. PRZM simulates pesticide application, movement and transformation on an agricultural field and the resultant pesticide loadings to a receiving water body via runoff, erosion and spray drift. EXAMS simulates the fate of the pesticide and resulting concentrations in the water body. The standard scenario used for ecological pesticide assessments assumes application to a 10-hectare agricultural field that drains into an adjacent 1-hectare water body, 2-meters deep (20,000 m^3 volume) with no outlet. PRZM/EXAMS was used to estimate screening-level exposure of aquatic organisms to pyroxasulfone residues. The measure of exposure for aquatic species is the 1-in-10 year return peak or rolling mean concentrations. The 1-in-10 year daily peak concentration is used for estimating acute exposures of direct effects to aquatic organisms as well as indirect effects. The 1-in-10-year 60-day mean concentration is used for assessing chronic exposure to fish. The 1-in-10 year 21-day mean concentration is used for assessing chronic exposures to aquatic invertebrates. Degradation products were not considered in the exposure modeling because of the persistence of pyroxasulfone. In addition, surface water modeling for total residues (parent+M1+M3) showed a small difference in exposure concentrations when compared with modeling for the parent.

Input Parameters
The appropriate input parameters were selected from the physical/chemical properties and environmental fate data submitted by the petitioner to support registration of pyroxasulfone (**Table 11**). Input parameters were selected in accordance with US EPA-OPP EFED water model parameter selection guidelines, Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides, Version 2.1, November 10, 2009. Expanded information about the models, selection of input parameters and scenarios can be obtained from http://www.epa.gov/oppefed1/models/water/index.htm.

Table 11. PRZM/EXAMS Modeling Inputs for Pyroxasulfone

Paremeter	Pyroxasulfone	Comment	Reference
Aerobic Soil Metabolism Half-life (days)	396.22	90th percentile of confidence bound of the mean N=10 Mean=343.8 days SD=119.8 days	47701736 47701737
Organic Carbon Partition Coefficient (K_{oc}) (mL/ g_{oc})	94.75	Average (104, 99, 119, 57)	47701742
Aerobic Aquatic Half-Life (days)	146.74	90th percentile of confidence bound of the mean N=2 Mean=108.5 days SD=0.7 days	47701740
Anaerobic Aquatic half-life (days)	71.94	90th percentile of confidence bound of the mean N=2 Mean=70.25 days SD=0.8 days	47701741
Aqueous Photolysis half-life (days)	119	Half-life value	47701734
Hydrolysis half-life (days)	Stable		47701733
Molecular Weight (g/mole)	367	Physical Property	
Henry's Law constant (atm-m^3/mol)	2.65E-9	Calculated	47701752
Water Solubility @ 25°C (mg/L)	3.49		47701752
Vapor Pressure (torr)	1.8E-8		47701752

Spray drift fractions were estimated to account for the required drift buffers on the V-10233 Herbicide Water Dispersible Granules Commercial and V-10233 Herbicide labels. The AgDrift model (version 2.01) was used to estimate the impact of spray drift buffers on drift fractions. It is important to recognize that the default aerial spray drift fraction (0.05) is greater than the adjusted spray fraction for the label recommended drift buffers. The edge-of-pond AgDrift model drift fraction is 0.1266. In contrast, the ground spray buffers for a low boom spray are consistent with the default drift fraction (0.01). Regardless of input parameters used, utilizing the buffers would reduce EECs.

Table 12. Spray Drift Fraction Used in Aquatic Exposure Modeling				
Buffer Size (ft)	**Spray**	**Default Spray Drift Fractions without a Buffer**	**AgDrift Spray Drift Fractions without a Buffer**	**Adjusted Spray Drift Fraction for Buffer**
9.8	Aerial	0.05	0.1266	0.109
40	Aerial	0.05	0.1266	0.081
9.8	Ground	0.01	0.0616	0.0091
32	Ground	0.01	0.0616	0.0137

PRZM/EXAMS scenario selection was focused on standard corn and wheat scenarios (**Table 13**). Because corn and soybeans is a common crop rotation, standard corn scenarios were selected to serve as surrogate scenarios for pyroxasulfone application on corn and soybeans. Agronomic practices including application rate, application timing, number of applications, application interval, and application method were modeled to represent proposed label practices. Fallowland use of pyroxasulfone was not explicitly modeled because the standard PRZM/EXAMS scenarios are associated with crops. Some proposed pyroxasulfone labels allow application to non-crop areas such as bare ground areas around orchards, vineyards, and farms. The surrogate scenarios used to model applications to non-crop areas were TN nursery, PA apple, and NY grapes. It is anticipated the EECs for fallowland will be represented in the range of modeled crop and non-crop uses. The corn scenarios apply to both corn and soybean uses. Because the pyroxasulfone products are applied by aerial or ground spray applications, the foliar chemical application method (CAM=2) was used in the exposure modeling.

Table 13: PRZM/EXAMS Simulated Application Rates, Method, and Timing According to Proposed Label							
Standard Scenario	**Label Application Time**	**Scenario Emerge Date (month-day)**	**PRZM Application Time (month-day)**	**Number of Apps**	**Application Interval**	**Spray Method**	**Application Rate (lbs/A)**
OH Corn	Preemerg	5-1	4-25	1	NA	Air	0.120
	Pre-plant		4-1	1/2	180	Ground	0.2136/0.1335
	Pre-plant (soil incorp)		4-16	1/2	180	Ground	0.2136/0.1335
	Post-emerg		5-15	1/2	180	Ground	0.2136/0.1335
	Fall		10-15	1	NA	Ground/Air	0.2136/0.120
IL Corn	Preemerg	5-1	4-25	1	NA	Air	0.120
	Pre-plant		4-1	1/2	180	Ground	0.2136/0.1335
	Pre-plant (soil incorp)		4-16	1/2	180	Ground	0.2136/0.1335
	Post		5-15	1/2	180	Ground	0.2136/0.1335
	Fall		10-15	1	NA	Ground/Air	0.2136/0.120
IA Corn	Preemerg	5-25	5-20	1	NA	Air	0.120
	Pre-plant		4-25	1/2	180	Ground	0.2136/0.1335
	Pre-plant (soil incorp)		5-5	1/2	180	Ground	0.2136/0.1335
	Post		6-1	1/2	180	Ground	0.2136/0.1335
	Fall		10-15	1	NA	Ground/Air	0.2136/0.120
MS Corn	Preemerg	4-10	4-5	1	NA	Air	0.120
	Pre-plant		3-10	1/2	180	Ground	0.2136/0.1335
	Pre-plant (soil incorp)		3-25	1/2	180	Ground	0.2136/0.1335
	Post		4-25	1/2	180	Ground	0.2136/0.1335
	Fall		11-15	1	NA	Ground/Air	0.2136/0.120
NDWheat	Pre-plant (Fall)		9-1	1	NA	Ground	0.1068
	Fall		9-1	1	NA	Ground	0.267
Non-Crop Use			NS	NS	NS	Ground	0.2625

Abbreviations: NA=not applicable, NS = not specified, post=post plant, preemerg=preemergent
1-180 days represent the label specified retreatment interval
Pre-plant = 30 day prior to emergence date
Pre-plant soil incorporated = 15 day prior emergence
Post-plant = 14 days post-emergence to V4 growth stage (corn) or an application date no later than June 1.
Rates represent a single application (spring)@ 0.2136 lbs ai/A and spring/fall application @ 0.1335 lbs ai/A. Labels state total application per crop cannot exceed 0.267 lbs ai/A.

Tier II- PRZM/EXAMS

Tier II estimated environmental concentrations for pyroxasulfone residues in surface water are shown in **Table 14**.

Table 14: Estimated Environmental Concentrations of Pyroxasulfone in Surface Water								
Standard Scenario	**Label Application Time**	**Number of Apps**	**Method of App**	**Spray Drift Buffer (feet)**	**App Rate (lbs/A)**	**Estimated Concentration (ug/L)**		
						1 in 10 yr Peak	**1 in 10 yr 21-day Average**	**1 in 10 yr 60-day Average**
IA Corn	Preemerg	1	Air	None	0.120	2.088	1.997	1.814
		1	Air	9.8	0.120	2.722	2.602	2.362
		1	Air	40	0.120	2.421	2.315	2.102
	Pre-plant	1	Ground	None	0.2136	2.072	2.021	1.901
		2	Ground	None	0.1335	2.498	2.441	2.292
	Pre-plant (soil incorp)	1	Ground	None	0.2136	1.583	1.523	1.411
		2	Ground	None	0.1335	1.635	1.582	1.470
	Post Plant	1	Ground	None	0.2136	1.508	1.443	1.325
		2		None	0.1335	3.031	2.973	2.300
	Fall	1	Ground	None	0.2136	3.441	3.375	3.251
		1	Air	None	0.120	2.538	2.484	2.392
		1	Air	9.8	0.120	3.240	3.165	3.042
		1	Air	40	0.120	2.097	2.841	2.732
IL Corn	Preemerg	1	Air	None	0.120	3.615	3.480	3.260
		1	Air	9.8	0.120	4.202	4.048	3.788
		1	Air	40	0.120	3.923	3.778	3.537
	Pre-plant	1	Ground	None	0.2136	7.271	7.090	6.938
		2	Ground	None	0.1335	7.832	7.635	7.400
	Pre-plant (soil incorp)	1	Ground	None	0.2136	3.304	3.218	3.039
		2	Ground	None	0.1335	3.198	3.102	2.969
	Post Plant	1	Ground	None	0.2136	7.271	7.090	6.938
		2		None	0.1335	7.382	7.635	7.400
	Fall	1	Ground	None	0.2136	5.821	5.730	5.556
		1	Air	None	0.120	2.281	2.223	2.150
		1	Air	9.8	0.120	2.912	2.845	2.734
		1	Air	40	0.120	2.613	2.554	2.456
OH Corn	Preemerg	1	Air	None	0.120	3.006	2.887	2.705
		1	Air	9.8	0.120	3.636	3.492	3.261
		1	Air	40	0.120	3.215	3.124	2.915
	Pre-plant	1	Ground	None	0.2136	5.980	5.788	5.567
		2	Ground	None	0.1335	6.172	5.973	5.648
	Pre-plant (soil incorp)	1	Ground	None	0.2136	1.927	1.857	1.724
		2	Ground	None	0.1335	2.034	1.970	1.842
	Post Plant	1	Ground	None	0.2136	5.980	5.788	5.567
		2		None	0.1335	6.172	5.973	5.648
	Fall	1	Ground	None	0.2136	3.990	3.891	3.833
		1	Air	None	0.120	2.859	2.787	2.735
		1	Air	9.8	0.120	3.542	3.450	3.373
		1	Air	40	0.120	3.218	3.135	3.070
MS Corn	Preemerg	1	Air	None	0.120	3.514	3.364	3.138
		1	Air	9.8	0.120	4.028	3.868	3.593
		1	Air	40	0.120	3.784	2.629	3.377
	Pre-plant	1	Ground	None	0.2136	8.388	8.137	7.641
		2	Ground	None	0.1335	8.341	8.115	7.779
	Pre-plant (soil incorp)	1	Ground	None	0.2136	3.489	3.346	3.091
		2	Ground	None	0.1335	3.618	3.484	3.268
	Post Plant	1	Ground	None	0.2136	8.388	8.137	7.641
		2		None	0.1335	8.341	8.115	7.779
	Fall	1	Ground	None	0.2136	7.308	7.198	5.833
		1	Air	None	0.120	6.737	6.579	5.800
		1	Air	9.8	0.120	7.307	7.131	6.291
		1	Air	40	0.120	7.037	6.868	6.057
NDWheat	Pre-plant (Fall)	1	Ground	None	0.1068	2.765	2.701	2.623
	Fall	1	Ground	None	0.267	6.912	6.752	6.557
Non-Crop Use								
TN Nursery		1	Ground	None	0.2625	4.002	3.883	3.645
PA apple		1	Ground	None	0.2625	2.254	2.171	2.020
NY grapes		1	Ground	None	0.2625	4.044	3.952	3.755

Uncertainty
There is a high percentage of applied radioactivity (8-25% of applied radioactivity) identified as unextracted soil/sediment residues. Because the extraction of pyroxasulfone residues was conducted using only acetonitrile/water without the use of sequentially harsher soil extractants, there is uncertainty regarding the identity and availability of the unextracted soil residues. The uncertainty with identification of unextracted residues is not expected to alter the exposure assessment because of the high persistence of pyroxasulfone,

Additionally, the major degradation product M1 is very persistent and mobile in laboratory and field studies. It is a potential groundwater contaminant because of the fate properties.

The aquatic exposure modeling was not conducted on fallow land use of pyroxasulfone. This modeling approach was taken because the PRZM/EXAMS standard scenarios represent scenarios with crops. It is anticipated the EECs for fallow land uses will be adequately represented by the exposure scenario for crops and non-crops uses.

b. Aquatic Exposure Monitoring and Field Data

Because pyroxasulfone is a new pesticide, there are no monitoring data in surface water and ground water.

c. Aquatic Bioaccumulation Assessment

Available data on the octanol-water partition coefficient (K_{ow}) for pyroxasulfone indicates that this pesticide has a low bioaccumulation potential in aquatic food webs. Because the log K_{ow} is < 4.0, KABAM v.1.0 was not used to estimate concentrations of pyroxasulfone in tissues of aquatic organisms resulting from bioaccumulation.

3. Measures of Terrestrial Exposure

a. Terrestrial Exposure Modeling

T-REX

Exposure of free-ranging terrestrial animals is a function of the timing and extent of pesticide application with respect to the location and behavior of those species. OPP's terrestrial exposure model generates exposure estimates assuming that the animal is present on the use site at the time that pesticide levels are highest. The upper-bound pesticide residue concentration on food items is calculated from both initial applications and any additional applications, taking into account pesticide degradation between applications. Although this approach is conservative, it is reasonable, particularly when considering acute risks. For acute risks, the assumption is that the duration of exposure is a single day and, again, occurs when residue levels are highest. In evaluating chronic risks, longer-term exposure estimates are also based on the assumption that the animal is present on the use site when residue levels are highest and furthermore that it repeatedly forages on the use site.

The current screening-level approach does not directly relate timing of exposure to critical or sensitive population, community, or ecosystem processes. Given that the application timing and location is crop-dependent, it is difficult to address the temporal and spatial co-occurrence of pyroxasulfone use and sensitive ecological processes. However, pesticides are frequently used from spring through fall; crop cultivation frequently starts in the spring, hence uses of pyroxasulfone are likely to occur in spring and perhaps summer depending on the region. Spring and early summer are typically seasons of active migrating, feeding, and reproduction for many wildlife species. The increased energy demands associated with these activities (as opposed to hibernation, for example) can increase the potential for exposure to pesticide-contaminated food items since agricultural areas can represent a concentrated source of relatively easily obtained, high-energy food items. In this assessment, the spatial extent of exposure for terrestrial animal species is limited to the use area only and the area immediately surrounding the use area.

Currently, the Agency does not require toxicity studies on reptiles and amphibians in support of pesticide registrations. To accommodate this data gap, birds are used as surrogates for terrestrial-phase amphibians and reptiles. It is assumed that, given the usually lower metabolic demands of reptiles and amphibians compared to birds, exposure to birds would be greater due to higher relative food consumption. The lack of toxicity data on reptiles and amphibians represents a source of uncertainty in this assessment.

Tables 15 and **16** list selected predicted EECs for birds, reptiles, terrestrial amphibians, and mammals obtained from T-REX simulations for the proposed uses of pyroxasulfone at the maximum *seasonal* label rates.

Table 15. Terrestrial Food-Item Residue Estimates for Birds with Pyroxasulfone Proposed Uses with a Foliar Dissipation Half-life default value of 35 Days.					
Crop	Food Item	Maximum Dose-Based EECs (mg/kg-bw)[1]	Maximum Dose-Based EECs (mg/kg-bw)[2]	Maximum Dose-Based EECs (mg/kg-bw)[3]	Dietary-Based EECs (mg/kg-diet)
Corn, soybean, winter wheat (0.267 lbs a.i./A)[a]	Short grass	72.98	41.62	18.63	64.08
	Tall grass	33.45	19.07	8.54	29.37
	Broadleaf plants/ small insects	41.05	23.41	10.48	36.05
	Fruits, pods, seeds, lg. insects	4.56	2.60	1.16	4.01
	Granivores	1.01	0.58	0.26	--
Non-crop sites (0.206 lbs a.i./A)[b]	Short grass	56.31	32.11	14.38	49.44
	Tall grass	25.81	14.72	6.59	22.66
	Broadleaf plants/ small insects	31.67	18.06	8.09	27.81
	Fruits, pods, seeds, lg. insects	3.52	2.01	0.90	3.09
	Granivores	0.78	0.45	0.20	--
Corn, soybean, fallow land, non-crop sites (0.120 lbs a.i./A)[c]	Short grass	32.80	18.70	8.37	28.80
	Tall grass	15.03	8.57	3.84	13.20
	Broadleaf plants/ small insects	18.45	10.52	4.71	16.20
	Fruits, pods, seeds, lg. insects	2.05	1.17	0.52	1.80
	Granivores	0.46	0.26	0.12	--
Soybean (0.096 lbs a.i./A)[d]	Short grass	26.24	14.96	6.70	23.04
	Tall grass	12.03	6.86	3.07	10.56
	Broadleaf plants/ small insects	14.76	8.42	3.77	12.96
	Fruits, pods, seeds, lg. insects	1.64	0.94	0.42	1.44
	Granivores	0.36	0.21	0.09	--

[1]Based on 20 gram birds
[2] Based on 100 gram birds
[3] Based on 1000 gram birds
[a] Single application at the maximum seasonal rate of 0.267 lbs a.i./A for corn, soybean, and winter wheat (KIH-485 W85 and Pyroxasulfone 85W labels)
[b] Single application at the maximum seasonal rate of 0.206 lbs a.i./A for non-crop sites (V-10233 Herbicide Water Dispersible Granules commercial label)
[c] Single application at the maximum seasonal rate of 0.120 lbs a.i./A for corn, soybean, fallow land, and non-crop sites (V-10233 Herbicide label)
[d] Single application at the maximum seasonal rate of 0.096 lbs a.i./A for soybean (V-10233 Herbicide Water Dispersible Granules commercial label)

Table 16. Terrestrial Food-Item Residue Estimates for Mammals with Pyroxasulfone Proposed Uses with a Foliar Dissipation Half-life default value of 35 Days.					
Crop	Food Item	Maximum Dose-Based EECs (mg/kg-bw)[1]	Maximum Dose-Based EECs (mg/kg-bw)[2]	Maximum Dose-Based EECs (mg/kg-bw)[3]	Dietary-Based EECs (mg/kg-diet)
Corn, soybean, winter wheat (0.267 lbs a.i./A)[a]	Short grass	61.10	42.23	9.79	64.08
	Tall grass	28.00	19.35	4.49	29.37
	Broadleaf plants/ small insects	34.37	23.75	5.51	36.05
	Fruits, pods, seeds, lg. insects	3.82	2.64	0.61	4.01
	Granivores	0.85	0.59	0.14	--
Non-crop sites (0.206 lbs a.i./A)[b]	Short grass	47.14	32.58	7.55	49.44
	Tall grass	21.60	14.93	3.46	22.66
	Broadleaf plants/ small insects	26.51	18.33	4.25	27.81
	Fruits, pods, seeds, lg. insects	2.95	2.04	0.47	3.09
	Granivores	0.65	0.45	0.10	--
Corn, soybean, fallow land, non-crop sites (0.120 lbs a.i./A)[c]	Short grass	27.46	18.98	4.40	28.80
	Tall grass	12.59	8.70	2.02	13.20
	Broadleaf plants/ small insects	15.45	10.67	2.48	16.20
	Fruits, pods, seeds, lg. insects	1.72	1.19	0.28	1.80
	Granivores	0.38	0.26	0.06	--
Soybean (0.096 lbs a.i./A)[d]	Short grass	21.97	15.18	3.52	23.04
	Tall grass	10.07	6.96	1.61	10.56
	Broadleaf plants/ small insects	12.36	8.54	1.98	12.96
	Fruits, pods, seeds, lg. insects	1.37	0.95	0.22	1.44
	Granivores	0.31	0.21	0.05	--

[1]Based on 15 gram mammal
[2] Based on 35 gram mammal
[3] Based on 1000 gram mammal
[a] Single application at the maximum seasonal rate of 0.267 lbs a.i./A for corn, soybean, and winter wheat (KIH-485 W85 and Pyroxasulfone 85W labels)
[b] Single application at the maximum seasonal rate of 0.206 lbs a.i./A for non-crop sites (V-10233 Herbicide Water Dispersible Granules commercial label)
[c] Single application at the maximum seasonal rate of 0.120 lbs a.i./A for corn, soybean, fallow land, and non-crop sites (V-10233 Herbicide label)
[d] Single application at the maximum seasonal rate of 0.096 lbs a.i./A for soybean (V-10233 Herbicide Water Dispersible Granules commercial label)

TERRPLANT

Effects on non-target terrestrial plants are most likely to occur as a result of spray drift and/or runoff from ground applications. These are important factors in characterizing the risk of pyroxasulfone to non-target plants, which is assumed to reach off-site soil. The TerrPlant (Ver.1.2.2) model predicts EECs for terrestrial plants located in dry and semi-aquatic areas adjacent to the treated field. The EECs are based on the application rate and solubility of the pesticide in water and drift characteristics. The amount of pyroxasulfone that runs off is a proportion of the application rate and is assumed to be 1%, based on pyroxasulfone's solubility of <10 ppm (i.e. 3.49 mg/L) in water. Drift from ground applications are assumed to be 1% the application rate; drift from aerial applications are assumed to be 5% the application rate. An incorporation depth was not referenced in the label, which meant setting the default value to 1 inch for ground applications. For a standard scenario on an agricultural field, the runoff scenario for terrestrial plants inhabiting dry areas adjacent to a field is characterized as "sheet runoff" (one treated acre to an adjacent acre; a 1:1 ratio) and inhabiting semi-aquatic areas adjacent to a field is characterized as "channelized runoff" (10 treated acre to an adjacent low-lying acre; a 10:1 ratio). The TerrPlant model EECs are presented in **Table 17.**

Table 17. Estimated Environmental Concentrations of Pyroxasulfone for Terrestrial Plants				
Application Method	**Application Rate (lbs a.i./A)***	**Dry areas (lb/A)[1]**	**Semi-Aquatic Areas (lb/A)[2]**	**Spray Drift (lb/A)[3]**
Ground	0.267	0.00534	0.02937	0.00267
Ground	0.206	0.00412	0.02266	0.00206
Ground	0.12	0.0024	0.0132	0.0012
Ground	0.096	0.00192	0.01056	0.00096
Aerial	0.12	0.0072	0.018	0.006

[1] EEC = Sheet Runoff + Drift (1% for ground or 5% for aerial)
[2] EEC = Channelized Runoff + Drift = 1% for ground or 5% for aerial
[3] EEC for ground (appl rate x 1% drift) and aerial (appl rate x 5% drift)
*Maximum *seasonal* application rates

Ground Water Modeling

To estimate exposure to plants when groundwater contaminated by pyroxasulfone is applied to crops, the following method was used. Predicted groundwater concentrations of pyroxasulfone (equivalent to the equilibrium concentration taken over a 30 year period) were used to estimate the potential phytotoxic effects from irrigation water to plants and sensitive crops on the treated field**.** It is assumed that a one-acre field is irrigated with one inch of water containing pyroxasulfone at the equilibrium concentration. Pyroxasulfone concentrations were estimated using a beta version of the PRZM GW Tier II model. This model is currently undergoing an implementation process in OPP. Model input parameters are shown in **Table 18**. The model provides ground concentrations as predicted through Pesticide Root Zone Model (PRZM) (**Table 19**).

Table 18. PRZM GW Tier II Model Input Parameters		
Input Parameter	**Value**	**Source**
Application Rate	0.267 lbs ai/A	Label
Hydrolysis Half-life	Stable	47701733
Soil Half-life	369 days	47701736 47701737
Koc	94.75	47701742

Table 19. GW Tier II Model and SCIGROW Estimated Pyroxasulfone in Groundwater and Estimated Concentrations in Soil from Irrigation Water			
Scenario	**Peak (ppb)**	**Post Breakthrough Average (ppb)**	**EECs (lbs a.i./A)[1]**
GA	33.3	28.7	0.007
FL Potato	46.7	38.2	0.009
FL Citrus	76.5	54.7	0.012
DE	94.1	83	0.019
NC	50.7	43.4	0.010
WI	181	149	0.034
SCIGROW	1.93		0

[1] EEC calculation: Assuming a one-acre field is irrigated with one inch of water containing pyroxasulfone. One acre has 6,272,640 cubic inches of water on the field. The1 acre field with 1 inch of water has 3,630 cubic ft of water (6,272,640 x 0.00058 cubic ft/cubic inch). The field has 27,156 gallons of water (3,630 cubic ft x 7.481 gallons/cubic ft). Therefore, 1 inch of water on the 1 acre field weighs 226,625 lbs (27,156 gallons x 8.3453 lbs/gallon of water).

$$\frac{226{,}625 \text{ lb of water/acre} * [\text{post breakthrough ave in ppb}]}{1{,}000{,}000{,}000} = \text{EEC in lbs a.i./A}$$

C. Ecological Effects Characterization

1. Aquatic Effects Characterization

a. Aquatic Animals

(1) Acute Effects

Freshwater Fish and Aquatic-Phase Amphibians -Technical

The freshwater fish studies on rainbow trout (*Oncorhynchus mykiss*, MRID 47701626) and bluegill sunfish (*Lepomis macrochirus*, MRID 47701627) are classified as acceptable limit tests. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Freshwater Fish and Aquatic-Phase Amphibians – Metabolites / Degradates

There are no acute data on metabolites/degradates for freshwater fish and aquatic- phase amphibians.

Freshwater Fish and Aquatic-Phase Amphibians -Formulations

There are no acute data on formulations for freshwater fish and aquatic-phase amphibians. Based on the proposed use pattern, aquatic EECs and lack of toxicity to freshwater fish at the limit of solubility, toxicity data on formulations (Technical End Use Products) would not be required.

Table 20. Freshwater Fish Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LC_{50}/NOAEC/LOAEC**	**MRID**	**Classification/ Category**
Technical KIH-485					
Rainbow trout *Oncorhynchus mykiss* (cold water species)	99.1	96 hour static renewal study (limit test) 3 reps / 10 fish per rep. Mean-measured: negative control (<LOQ = 0.28 mg a.i./L), 2.2 mg a.i./L	96-hr LC_{50} > **2.2**[2] mg a.i./L NOAEC ≥ 2.2 mg a.i./L Endpoint(s) affected: None. *Sublethal effects:* None.	47701626	Acceptable At most moderately toxic[1]
Bluegill sunfish *Lepomis macrochirus* (warm water species)	99.1	96 hour static renewal study (limit test) 3 reps / 10 fish per rep. Mean-measured: negative control (<LOQ = 0.28 mg a.i./L), 2.8 mg a.i./L	96-hr LC_{50} > 2.8 mg a.i./L NOAEC ≥ 2.8 mg a.i./L Endpoint(s) affected: None. *Sublethal effects:* None.	47701627	Acceptable At most moderately toxic[1]

[1]Based on LC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic
[2] **Bold** values used in risk description

Freshwater Invertebrates -Technical
The freshwater invertebrate study using the technical grade active ingredient on water flea (*Daphnia magna*, MRID 47701623) is classified as an acceptable limit test. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Freshwater Invertebrates –Metabolites / Degradates
There are no acute data on metabolites/degradates for freshwater invertebrates.

Freshwater Invertebrates –Formulations
There are no acute data on formulations for freshwater invertebrates. Based on the proposed use pattern, aquatic EECs and lack of toxicity to freshwater invertebrates at the limit of solubility, toxicity data on formulations (Technical End Use Products) would not be required.

Table 21. Freshwater Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**EC_{50}/NOAEC/LOAEC**	**MRID**	**Classification / Category**
Technical KIH-485					
Water flea *Daphnia magna*	Not provided (possibly ≥ 98.1% w/w)	48 hour static study (limit test) 4 reps per test group, 2 reps per control group; 10 invertebrates per rep Mean-measured: Negative control (<LOQ = 0.000022 mg a.i./L), 4.4[3] mg a.i./L	48-hr EC_{50} > **4.4**[2] mg a.i./L 48-hr NOAEC ≥ 4.4 mg a.i./L Endpoint(s) affected: None. Endpoint(s) considered: immobility, adverse reactions *Sublethal effects:* None.	47701623	Acceptable At most, Moderately toxic[1]
[1]Based on EC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic [2] **Bold** values used in risk description [3] On account of this test compound being poorly soluble, the test was conducted at the solubility limit for the compound using the column elution method to achieve saturation.					

Marine/Estuarine Fish – Technical

A definitive marine/estuarine fish study using the technical grade active ingredient on sheepshead minnow *Cyprinodon variegatus* (MRID 47701628) is classified as acceptable. The NOAEC ≥ 3.3 mg a.i./L and the EC_{50} > 3.3 mg a.i./L because no treatment related effects were observed at the highest test concentration. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Marine/Estuarine Fish – Metabolites/Degradates

There are no acute data on metabolites/degradates for marine/estuarine fish.

Marine/Estuarine Fish – Formulations

There are no acute data on formulations for marine/estuarine fish. Based on the proposed use pattern, aquatic EECs and lack of toxicity to marine/estuarine fish at the limit of solubility, toxicity data on formulations (Technical End Use Products) would not be required.

Table 22. Marine/ Estuarine Fish Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LC_{50}/NOAEC/LOAEC**	**MRID**	**Classification/ Category**
Technical KIH-485					
Sheepshead Minnow *Cyprinodon variegatus*	99.1	96-hour flow-through study 2 reps; 10 fish per rep.; 20 fish per test concentration Mean-measured: Negative control (<LOQ = 0.1 mg a.i./L), DMF, 0.29, 0.59, 1.2, 2.0, and 3.3 mg a.i./L	96-hr LC_{50} > **3.3**[2] mg a.i./L 96-hr NOAEC ≥ 3.3 mg a.i./L Endpoint(s) affected: None. Endpoint(s) considered: mortality. *Sublethal effects:* None.	47701628	Acceptable/ At most, moderately toxic[1]

[1]Based on LC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic
[2] **Bold** values used in risk description

Marine/Estuarine Invertebrates – Technical
A definitive marine/estuarine invertebrate study using the technical grade active ingredient on eastern oyster *Crassostrea virginica* (MRID 47701624) is classified as acceptable. The NOAEC ≥ 3.6 mg a.i./L and the EC_{50} > 3.6 mg a.i./L because no treatment related effects were observed at the highest test concentration. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description. However, only one replicate was used per treatment and in each control. Guidance recommends a minimum of two replicates of 10 oysters in each replicate for a total of 20 oysters per treatment and in each control. An EC_{50} and NOAEC are not calculable since linear regression indicates no dose-response and estimation of any parameter using this method would likely be an under-estimation (i.e., less protective or conservative estimate) of true sensitivity.

The marine/estuarine invertebrate study using the technical grade active ingredient on saltwater mysid *Americamysis bahia* (MRID 47701625) is classified as supplemental because results of a range-finding test which would determine the most sensitive age for testing was not reported. Nevertheless, juveniles (28-45 hours old) were used for testing. Current guidance suggests using juveniles <24 hours old or young adults 5-6 days old, depending on range-finding test results. Juveniles used in this test yielded a NOAEC ≥ 1.4 mg a.i./L and an LC_{50} >1.4 mg a.i./L. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Marine/Estuarine Invertebrates – Metabolites/Degradates
There are no acute data on metabolites/degradates for marine/estuarine invertebrates.

Marine/Estuarine Invertebrates – Formulations
There are no acute data on formulations for marine/estuarine invertebrates. Based on the proposed use pattern, aquatic EECs and lack of toxicity to marine/estuarine invertebrates at the limit of solubility, acute toxicity data on formulations (Technical End Use Products) would not be required.

Table 23. Marine/ Estuarine Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**EC_{50}/LC_{50}/NOAEC/LOAEC**	**MRID**	**Classification/ Category**
Technical KIH-485					
Eastern oyster *Crassostrea virginica*	99.1	96 hour flow-through study 20 bivalves per level (1 replicate)* Mean-measured: negative control (<LOQ = 0.1 mg a.i./L), DMF, 0.30, 0.60, 1.2, 2.1, and 3.6[3] mg ai/L * Guidance recommends a minimum of two replicates of 10 oysters in each replicate for a total of 20 oysters per treatment and in each control. *An EC_{50} and NOAEC are effectively not calculable since linear regression indicates no dose-response and estimation of any parameter using this method would likely be an under-estimation (i.e., less protective or conservative estimate) of true sensitivity.*	96-hr $EC_{50} > 3.6$ mg a.i./L NOAEC ≥ 3.6 mg a.i./L Endpoint(s) affected: None. Endpoints considered: mortality, shell deposition (at 96 hours) *Sublethal effects:* None.	47701624	Acceptable / At most, moderately toxic[1]

Table 23. Marine/ Estuarine Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**EC_{50}/LC_{50}/NOAEC/LOAEC**	**MRID**	**Classification/ Category**
Saltwater mysid *Americamysis bahia*	99.1	96 hour flow-through study 2 reps.;10 mysids per rep.; 20 mysids per treatment Mean-measured: negative control (<LOQ = 0.05 mg a.i./L), DMF, 0.083, 0.17, 0.34, 0.68, and 1.4 mg ai/L	96-hr LC_{50} > **1.4**[2] mg a.i./L NOAEC ≥ 1.4 mg a.i./L Endpoint(s) affected: None. Endpoint(s) considered: mortality *Mortality* One mortality was observed in the 0.083 mg a.i./L mean-measured treatment group, but was not dose-responsive and so was not considered to be treatment related. *Sublethal effects:* None.	47701625	Supplemental / At most, moderately toxic[1]

[1]Based on EC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic
[2] **Bold** values used in risk description
[3] Apparent solubility limit in saltwater was not reported. Stated to be the highest concentration tested. On account of this test compound being poorly soluble, precipitate was observed in the 2.5 and 5.0 mg a.i./L treatment group test chambers. As a result, analytical methodology included centrifugation of samples per Guideline 850.1000.

(2) Chronic Effects

Freshwater Fish and Aquatic-Phase Amphibians – Technical

The early life-cycle freshwater fish study on fathead minnow (*Pimephales promelas*, MRID 47701630) is classified as acceptable. The growth endpoints (wet weight and length) of surviving fish (which were used in the study since <24 hours old) at the end of the exposure period (28-days) indicated statistically significant reductions (Dunnett's test, p = 0.05) in the highest test concentration leading to a NOAEC of 2.0 mg a.i./L and LOAEC of 3.9 mg a.i./L. The growth endpoint for dry weight of surviving fish did not show statistically significant reductions at any level.

Hatching occurred at all levels on Days 4 and 5. Hatching success was 98% in the negative and solvent control groups and was at 99-100% for all treatment levels, with no statistically significant differences observed. Post-hatch survival (28-days post-hatch) in both the negative and solvent controls was 90% at test termination. Larval survival in the mean-measured test concentrations 0.30, 0.58, 1.2, 2.0, and 3.9 mg a.i./L was 93, 76, 89, 91, and 89%, respectively. The 14% reduction observed in the 0.58 mg a.i./L mean measured test concentration (from the negative control with 90% survival) was statistically significantly different (Dunnett's test, p = 0.05; MSD[3] value of 9.1%) relative

[3] MSD = minimum significant difference

to the negative control, but was not considered treatment related as higher concentrations did not exhibit similar or increasing effects to the test compound.

Most organisms appeared normal in the control and treatment groups. Weakness, small size, and a curled/crooked spine were also observed; the frequency of occurrence of abnormalities in the treatment groups did not appear to differ greatly from the controls.

Freshwater Fish and Aquatic-Phase Amphibians –Metabolites / Degradates
There are no chronic data on metabolites/degradates for freshwater fish and aquatic-phase amphibians.

Freshwater Fish and Aquatic-Phase Amphibians –Formulations
There are no chronic data on formulations for freshwater fish and aquatic- phase amphibians, as these data are not required.

Table 24. Freshwater Fish Chronic Toxicity Data

Common Name	%AI	Study parameters	NOAEC/LOAEC	MRID	Classification /Category
Technical KIH-485					
Fathead minnow *Pimephales promelas*	99.1	28-day flow-through early life-stage test 80 embryos per level, split into 20 embryos per cup, 1 cup per aquarium, 4 rep. aquaria per treatment Mean-measured: Negative control (<LOQ = 0.10 mg a.i./L), DMF control, 0.30, 0.58, 1.2, 2.0, and 3.9[2] mg a.i./L	28-day NOAEC: **2.0**[1] mg a.i./L 28-day LOAEC: 3.9 mg a.i./L Most sensitive endpoint: wet weight, length *Additional endpoints affected:* A significant reduction in percent survival relative to the controls was observed in the 0.58 mg a.i./L mean measured concentration, but was not considered treatment related as higher concentrations did not exhibit similar or increasing effects to the test compound. *Sublethal effects:* Most organisms appeared normal in the control and treatment groups. Weakness, small size, and a curled/crooked spine were also observed; the frequency of occurrence of abnormalities in the treatment groups did not appear to differ greatly from the controls.	47701630	Acceptable

[1]**Bold** used in risk quotient calculations
[2] Reported solubility limit in freshwater: < 5.0 mg a.i./L (likely approximates the highest mean-measured concentration tested ~3.9 mg a.i./L)

Freshwater Invertebrates – Technical
A chronic freshwater invertebrate study (MRID 47701629) with pyroxasulfone technical (99.1%) is classified as acceptable. Statistically analyzed endpoints (Dunnett's test, $p>0.05$) including first-generation Daphnid survival, reproduction (number of live young produced per reproductive day), and growth (length and dry weight at day 21), indicated no statistically significant difference from pooled control, negative control, and solvent control. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Freshwater Invertebrates –Metabolites / Degradates
There are no chronic data on metabolites/degradates for freshwater invertebrates.

Freshwater Invertebrates –Formulations
There are no chronic data on formulations for freshwater invertebrates, as these data are not required.

Table 25. Freshwater Invertebrate Chronic Toxicity Data					
Common Name	**%AI**	**Study parameters**	**NOAEC/LOAEC**	**MRID**	**Classification /Category**
Technical KIH-485					
Water flea *Daphnia magna*	99.1	21-day flow-through test 2 reps. per treatment and control group; 10 Daphnids per rep; 20 Daphnids per treatment Mean-measured: Negative control (<LOQ = 0.03 mg a.i./L), DMF control, 0.05, 0.13, 0.30, 0.77, and 1.9 mg a.i./L	NOAEC ≥ **1.9**[1] mg a.i./L LOAEC > 1.9 mg a.i./L Endpoint(s) affected: None. Endpoint(s) considered: 1st generation survival, reproduction (number of live young produced per reproductive day), and growth Sublethal effects: Discoloration (pale), injury, and lethargy were infrequent, comparable to controls, and not considered treatment related.	47701629	Acceptable
[1] **Bold** value used in risk description.					

Marine/Estuarine Fish
No chronic marine/estuarine fish studies were submitted for review.

Marine/Estuarine Invertebrates
No chronic marine/estuarine invertebrate studies were submitted for review.

b. Aquatic Plants

Vascular Aquatic Plants - Technical
The vascular aquatic plant study (MRID 47701640) on duckweed (*Lemna gibba*) is classified as supplemental because of a major guideline deviation. A small amount of test material (0.0405 µg a.i./L) was detected in the solvent control at test initiation, which is slightly above the limit of quantitation (0.0255 µg a.i./L); none was detected at test termination. Contamination of controls with the test substance is reason to question the validity of the study (per OPPTS 850.4400). However, there were no statistically significant differences between the negative and solvent control groups when compared using a two-tailed Student's t-test (p=0.05). In addition, EFED guidance indicates that statistically significant differences be determined between only the negative control and the treatment groups, which implies that endpoint calculations would not be affected as a result. Indeed, endpoint calculations indicate that statistically significant effects (relative to the negative control) were observed at concentrations just beyond the lowest level tested (*i.e.*, 7-day NOAEC = 0.18 µg a.i./L based on frond count). In addition, the 7-day EC_{50} is 6.0 µg a.i./L based on frond count.

Vascular Aquatic Plants – Metabolites/ Degradates
The two metabolite vascular aquatic plant studies (MRID 47701641 on M-1; and, MRID 47701642 on M-3) on duckweed (*Lemna gibba*) are classified as acceptable. Statistically significant growth inhibition was not detected at any test level relative to the negative control for either study leading to a 7-day NOAEC of ≥123 mg a.i./L and 7-day EC_{50} of >123 mg a.i./L. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

Vascular Aquatic Plants – Formulations
There are no data on formulations for vascular aquatic plants, as these data are not required.

Non-vascular Aquatic Plants - Technical
The non-vascular aquatic plant study on freshwater green algae *Pseudokirchneriella subcapitata* (MRID 47701643) is classified as supplemental (but upgradable) on account of high variability in analytic recovery of test samples, which were attributed to chromatographic interference. As a result, nominal concentrations were used to determine the endpoints (96-hour EC_{50} 0.00038 mg a.i./L based on cell density; 96-hour NOAEC 0.00005 mg a.i./L based on biomass). If raw laboratory results for the quantities and volumes used to make up the solutions are provided (*i.e.*, information beyond the study Appendix I 'Verification of Test Concentrations' where it is indicated that the presence of algae significantly affected the test chemical recovery), then the study can be upgraded. The raw data would serve as a record to confirm the expected nominal concentrations in addition to analytical results at levels above where interference affects analytical detection. In addition, random assignment of treatments and test vessels were not reported in the test protocol; this information would also be required for the study to be upgradable.

The non-vascular aquatic plant study on freshwater blue-green algae/cyanobacteria *Anabaena flos-aquae* (MRID 47701644) is classified as acceptable. All three endpoints (cell density, biomass, and growth rate) yielded a 96-hour EC_{50} >3.5 mg a.i./L (as this endpoint is non-definitive, it is not useful for RQ calculations, but can contribute to risk description); cell density and growth rate yielded NOAECs of 0.16 mg a.i./L and biomass yielded a NOAEC of 1.6 mg a.i./L.

Similarly, the non-vascular aquatic plant study on freshwater diatom *Navicula pelliculosa* (MRID 47701645) is classified as acceptable. All three endpoints (cell density, biomass, and growth rate) yielded a 96-hour EC_{50} > 3.2 mg a.i./L and NOAEC $\geq$ 3.2 mg a.i./L. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

The non-vascular aquatic plant study on marine diatom *Skeletonema costatum* (MRID 47701646) is classified as supplemental. The reason being that after 96 hours, the increase in cell density was approximately 14 times, resulting in a cell density of ~ 1.1×10^6 cells/mL in the controls. This is slightly less than the OPPTS 850.5400 guideline requirement that cell density should reach 1.5×10^6 cells/mL at 96 hours to demonstrate logarithmic growth. Although the guideline requirement was not met, the final cell density was only marginally below that required and inhibition of algal growth was demonstrated during the exposure to pyroxasulfone. However, due to the growth in the controls not being fully exponential some uncertainty exists to the accuracy of the results obtained. All three endpoints (cell density, biomass, growth rate) yielded a NOAEC of 0.14 mg a.i./L; the most sensitive endpoint on the basis of EC_{50} (= 0.66 mg a.i./L) is cell density.

Non-vascular Aquatic Plants – Metabolites / Degradates
The non-vascular aquatic plant study on freshwater green algae *Pseudokirchneriella subcapitata* (MRID 47701647) with metabolite M-1 (97.54% a.i.) is classified as supplemental on account of pH values that deviated from guideline recommendations and neutral levels. More specifically, the pH values were above and below the guideline recommended value (7.5 ± 0.1) for *P. subcapitata*. The values were higher at test termination (8.0-8.1) than they were at test initiation (6.1-7.8) for the control and all concentrations except the highest concentration, which had the lowest pH values (3.8, 3.9) for the two observation times. All three endpoints (cell density, biomass, growth rate) yielded a NOAEC of 31 mg a.i./L; the most sensitive endpoint on the basis of EC_{50} (= 56 mg a.i./L) is cell density.

Similarly, the non-vascular aquatic plant study on freshwater green algae *Pseudokirchneriella subcapitata* (MRID 47701648) with metabolite M-3 (99.6 % a.i.) is classified as supplemental on account of pH values that deviated from guideline recommendations and neutral levels. More specifically, the pH values were above and below the guideline recommended value (7.5 ± 0.1) for *P. subcapitata.* The values were higher at test termination (8.5-8.9) than they were at test initiation (6.9-7.4) for the control and all concentrations except the two highest concentrations, which had the lowest pH values (4.9, 6.5 for 61 mg a.i/L; 3.6, 4.2 for 123 mg a.i./L) for the two observation times (initiation, termination, respectively). All three endpoints (cell density, biomass, growth rate) yielded a NOAEC of 15 mg a.i./L; the most sensitive endpoint on the basis of EC_{50} (= 38 mg a.i./L) is cell density.

Non-vascular Aquatic Plants – Formulations
There are no data on formulations for non-vascular aquatic plants, as these data are not required.

Table 26. Aquatic Plant Toxicity Data

Species	%A.I.	Study Parameters	EC_{50}/NOAEC	MRID No.	Study Classification
Technical KIH-485					
Vascular Aquatic Plants					
Duckweed *Lemna gibba G3*	98.1	Tier II study 7 day static study 3 reps. / 4 plants (12 fronds) per rep. Mean measured: Negative control (<LOQ = 0.0255 μg a.i./L), DMF control, 0.075, 0.18, 0.43, 1.0, 2.3, 5.2, 12, 27 μg a.i./L	Frond count 7-day EC_{50}: **6.0**[1] (4.9-7.3) μg a.i./L 7-day NOAEC: **0.18**[3] μg a.i./L Biomass 7-day EC_{50}: 9.0 (6.5-13) μg a.i./L 7-day NOAEC: 0.43 μg a.i./L Growth rate (based on frond number) 7-day EC_{50}: 16 (15-17) μg a.i./L 7-day NOAEC: 1.0 μg a.i./L Most sensitive endpoint: frond count based on EC_{50} and NOAEC Endpoint(s) affected: frond count, biomass, growth rate (based on frond number) *Sublethal effects*: Root destruction and curled fronds were noted in the 2.3 μg a.i./L treatment level, while root destruction, curled fronds, and small fronds were noted in the 5.2, 12, and 27 μg a.i./L treatment levels. A marked increase in chlorotic and necrotic fronds were noted in the 5.2, 12, and 27 μg a.i./L test levels. Appearance of chlorotic and necrotic plants increased over the duration of the study.	47701640	Supplemental
Metabolites/ Degradates					

Table 26. Aquatic Plant Toxicity Data					
Species	**%A.I.**	**Study Parameters**	**EC_{50}/NOAEC**	**MRID No.**	**Study Classification**
Vascular Aquatic Plants					
Duckweed *Lemna gibba G3*	97.54% M-1	Tier II study 7 day static renewal study 3 reps. / 4 plants (12 fronds) per rep. Mean measured: Negative control (<LOQ = 4.0 mg a.i./L), 7.7, 16, 31, 61, and 123 mg a.i./L	Frond count, biomass, growth rate (based on frond number and biomass): 7-day EC_{50} > **123**[2] mg a.i./L 7-day NOAEC ≥ 123 mg a.i./L Endpoint(s) affected: None. *(Sub)lethal effects*: Duckweed plants in each control replicate exhibited normal growth throughout the test. After 7 days of exposure, the percent of chlorotic fronds observed on the plants in the negative control and the 31 and 61 mg a.i./L treatment groups was 0.51, 0.43, and 0.22% of the total number of fronds, respectively. The percent of necrotic fronds in the 7.7, 31, 61, and 123 mg a.i./L was 0.58, 0.47, 0.22, and 0.20% of the total fronds, respectively. Mortality in the 7.7, 61, and 123 mg a.i./L was 0.22, 0.23, and 0.38% of the total fronds, respectively. The percentage of dead, chlorotic, and necrotic fronds increased over the duration of the study.	47701641	Acceptable

Table 26. Aquatic Plant Toxicity Data					
Species	**%A.I.**	**Study Parameters**	**EC_{50}/NOAEC**	**MRID No.**	**Study Classification**
Duckweed *Lemna gibba G3*	99.6% M-3	Tier II study 7 day static renewal study 3 reps. / 4 plants (12 fronds) per rep. Mean measured: Negative control (<LOQ = 4.0 mg a.i./L), 7.6, 16, 31, 60, and 123 mg a.i./L	Frond count, biomass, growth rate (based on frond number and biomass): 7-day EC_{50} > **123**[2] mg a.i./L 7-day NOAEC ≥ 123 mg a.i./L Endpoint(s) affected: None. *(Sub)lethal effects*: Duckweed plants in each control replicate exhibited normal growth throughout the test. After 7 days of exposure, the percent of chlorotic fronds observed on the plants in the negative control and the 7.6, 16, 31, and 123 mg a.i./L treatment groups was 0.16, 0.18, 0.19, 0.34, and 0.39% of the total number of fronds, respectively. The percent of necrotic fronds in the negative control and the 7.6, 16, 31, 60 mg a.i./L treatment groups was 0.16, 0.54, 0.58, 0.17, and 0.77% of the total fronds, respectively. Dead fronds were observed only in the 123 mg a.i./L treatment group (on day 7 only) with the percent mortality of 0.19% of the total fronds. Chlorosis and necrosis was observed by day 5; the percentage observed with these characteristics increased by day 7.	47701642	Acceptable
Technical KIH-485					
Non-Vascular Aquatic Plants					

Table 26. Aquatic Plant Toxicity Data

Species	%A.I.	Study Parameters	EC_{50}/NOAEC	MRID No.	Study Classification
Freshwater Green Algae *Pseudokirchneriella subcapitata*	99.1	Tier II study 96-hour static study 3 reps. Nominal concentrations*: negative control (<LOQ = 0.000022 mg a.i./L), 0.00005, 0.0001, 0.0002, 0.0004, and 0.0008 mg a.i./L *Mean measured concentrations were highly variable; justified by study authors as resulting from chromatographic interference	Cell density: 96-hr EC_{50}: **0.00038**[1] (0.00035-0.00041) mg a.i./L 96-hr NOAEC: **0.0001**[3] mg a.i./L Biomass: 96-hr EC_{50} > 0.0008 mg a.i./L 96-hr NOAEC: 0.00005 mg a.i./L Growth rate 96-hr EC_{50}: 0.00077 (0.00073-0.00082) mg a.i./L 96-hr NOAEC: 0.0002 mg a.i./L Most sensitive endpoint: Cell density (EC_{50}), biomass (NOAEC) Endpoint(s) affected: cell density, biomass, growth rate *Sublethal effects:* There were no abnormalities detected in any of the control or test cultures.	47701643	Supplemental (but upgradable)

Table 26. Aquatic Plant Toxicity Data					
Species	**%A.I.**	**Study Parameters**	**EC_{50}/NOAEC**	**MRID No.**	**Study Classification**
Freshwater Blue-green algae *Anabaena flos-aquae*	98.1	Tier II study 96-hour static study 3 reps. Mean-measured: Negative control (<LOQ = 0.102 mg a.i./L), DMF, 0.16, 0.35, 0.80, 1.6, and 3.5 mg a.i./L	Cell density: 96-hr EC_{50} >3.5 mg a.i./L 96-hr NOAEC: 0.16 mg a.i./L Growth rate 96-hr EC_{50} > 3.5 mg a.i./L 96-hr NOAEC: 0.16 mg a.i./L Biomass: 96-hr EC_{50} > 3.5 mg a.i./L 96-hr NOAEC: 1.6 mg a.i./L Most sensitive endpoint: Cell density and growth rate (on the basis of the NOAEC) Endpoint(s) affected: cell density, growth rate, biomass *Sublethal effects:* Cell aggregation and long chains were observed in all treatment levels and controls.	47701644	Acceptable
Freshwater Diatom *Navicula pelliculosa*	98.1	Tier II study 96-hour static study 4 reps. Mean measured: Negative control (<LOQ = 0.204 mg a.i./L), DMF, 0.23, 0.47, 0.97, 1.8, and 3.2 mg a.i./L	Cell density, biomass, growth rate: 96-hour EC_{50} > 3.2 mg a.i./L 96-hour NOAEC $\geq$ 3.2 mg a.i./L Endpoint(s) affected: None. *Sublethal effects:* Cell aggregation was observed in all treatment levels and controls.	47701645	Acceptable

Table 26. Aquatic Plant Toxicity Data					
Species	**%A.I.**	**Study Parameters**	**EC_{50}/NOAEC**	**MRID No.**	**Study Classification**
Marine Diatom *Skeletonema costatum*	98.1	Tier II study 96-hour static study 3 reps. Mean measured: negative control (<LOQ = 0.0102 mg a.i./L), DMF, 0.013, 0.029, 0.063, 0.14, 0.30, 0.68, 1.4, and 2.9 mg/L	Cell density: 96-hr EC_{50}: 0.66 (0.4-1.1) mg a.i./L 96-hr NOAEC: 0.14 mg a.i./L Biomass: 96-hr EC_{50} > 2.9 mg a.i./L 96-hr NOAEC: 0.14 mg a.i./L Growth rate 96-hr EC_{50} > 2.9 mg a.i./L 96-hr NOAEC: 0.14 mg a.i./L Most sensitive endpoint: Cell density (based on EC_{50}) Endpoint(s) affected: cell density, biomass, growth rate *Sublethal effects:* There was evidence of cell aggregation in all treatment levels without significant growth inhibition including the controls. Because aggregation is typically observed with higher cell density, this observation was not considered to be a treatment related effect.	47701646	Supplemental
Metabolites / Degradates					
Non-Vascular Aquatic Plants					

Table 26. Aquatic Plant Toxicity Data					
Species	**%A.I.**	**Study Parameters**	**EC_{50}/NOAEC**	**MRID No.**	**Study Classification**
Freshwater Green Algae *Pseudokirchneriella subcapitata*	97.54 M-1	Tier II study 96 hour static study 3 reps Mean-measured: Negative control (<LOQ = 4.0 mg a.i./L), 7.9, 16, 31, 61, and 122 mg a.i./L	Cell density EC_{50}: **56**[1] (47-67) mg a.i./L NOAEC: **31**[3] mg a.i./L Growth rate EC_{50}: 78 (68-89) mg a.i./L NOAEC: 31 mg a.i./L Biomass EC_{50} > 120 mg a.i./L NOAEC: 31 mg a.i./L Most sensitive endpoint: cell density Endpoint(s) affected: cell density, growth rate, biomass *Sublethal effects*: None.	47701647	Supplemental
Freshwater Green Algae *Pseudokirchneriella subcapitata*	99.6 M-3	Tier II study 96-hour static study 3 reps. Mean-measured: Negative control (<LOQ = 4.0 mg a.i./L), 7.0, 15, 32, 61, and 123 mg a.i./L	Cell density EC_{50}: **38**[1] (2.2-670) mg a.i./L NOAEC: **15**[3] mg a.i./L Growth rate EC_{50}: 40 ($3.6x\ 10^{-21} – 4.4x10^{23}$) mg a.i./L NOAEC: 15 mg a.i./L Biomass EC_{50} > 120 mg a.i./L NOAEC: 15 mg a.i./L Most sensitive endpoint: cell density Endpoint(s) affected: cell density, growth rate, biomass *Sublethal effects*: None.	47701648	Supplemental

[1]**Bold** value used in risk quotient calculation for non-listed plant species whereby RQ = EEC/EC_{50}
[2]**Bold** value used in risk description for non-listed (EC_{50} value) and listed (NOAEC value) plant species
[3]**Bold** value used in risk quotient calculation for listed plant species whereby RQ = EEC/NOAEC

Non-vascular Aquatic Plants (Non-guideline study) – Technical

The non-vascular aquatic plant study on freshwater green algae *Pseudokirchneriella subcapitata* (MRID 47701751) on technical grade pyroxasulfone (99.1% a.i.) is classified as supplemental given it is a non-guideline study. In addition, a negative (untreated) control was not included in the study; only a solvent control was used for comparison with a single test treatment concentration. It is also unclear from the study protocol why a test concentration (nominal) of 2 μg a.i./L was used in the study. The study was intended to assess the recovery potential of the green algae after a 72-hour exposure period. According to the study authors and primary reviewer (APVMA) re-calculations of growth rate the effect of pyroxasulfone on green algae (*P. subcapitata*) was algistatic rather than algicidal at the tested concentration (2.13 μg a.i./L).

Table 27. Aquatic Plant Toxicity Data: Non-guideline studies					
Species	**%A.I.**	**Study Parameters**	**Endpoint**	**MRID No.**	**Study Classification**
Technical KIH-485					
Non-vascular Aquatic Plants					
Freshwater green algae *Pseudokirchneriella subcapitata*	99.1	Algicidal vs. algistatic effects static study 72-hour exposure phase; 144-hour recovery phase 3 reps. Mean measured: DMF, 2.13 μg a.i./L	% Inhibition of growth rate: 51.4% during exposure phase	47701751	Supplemental

2. Terrestrial Effects Characterization

a. Terrestrial Animals

(1) Acute Effects

Birds – Technical

The acute avian oral studies (MRID 47701631, 47701632) on 23-week old Northern bobwhite quail (*Colinus virginianus*) and zebra finch (*Poephila guttata*) of unspecified age, respectively, assessed over 14 days are classified as acceptable. KIH-485 Technical was administered to the birds via gavage (single dose of test substance in corn oil orally intubated into the crop or proventriculus of the bird) at nominal levels of 0 (negative control), 292, 486, 810, 1350, and 2250 mg a.i./kg-bw for the bobwhite study and only 0 (negative control) and 2250 mg a.i./kg-bw for the zebra finch (a limit test). The 14-day acute oral LD_{50} from both studies was >2250 mg ai/kg bw; similarly, the 14-day NOAEL ≥2250 mg ai/kg bw. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description. The quail study indicated no mortalities, overt signs of toxicity, or treatment-related effects on body weight or food consumption at the dosage levels tested. The finch study indicated no mortalities or overt signs of toxicity in the single treatment group tested, there were no apparent treatment-related effects upon body weight, and the estimated food consumption over the duration of the study was not reported. KIH-485 Technical (pyroxasulfone) would be classified as practically non-toxic to young adult Northern bobwhite quail (*C. virginianus*) as well as to zebra finch (*P. guttata*) of unspecified age in accordance with the classification system of the U.S. EPA.

The acute avian dietary studies (MRID 47701633, 47701634) on 10-day old Northern bobwhite quail (*Colinus virginianus*) and 9-day old mallard duck (*Anas platyrhynchos*), respectively, assessed over 8 days are classified as acceptable. KIH-485 Technical was administered to the birds in the diet at nominal concentrations of 0 (negative control), 562, 1000, 1780, 3160, and 5620 mg a.i./kg-diet. The 8-day acute dietary LC_{50} is >5620 mg a.i./kg diet and the 8-day NOAEC is ≥ 5620 mg a.i./kg-diet for the quail study. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description. The quail study indicated no mortalities, overt signs of toxicity, or treatment-related effects on body weight or food consumption at the dosage levels tested. The 8-day acute dietary LC_{50} is also >5620 mg a.i./kg diet for the duck study. However, relative to the control, the highest two treatment groups 3160 and 5620 mg a.i./kg-diet had a reduced increase in body weight that was significantly different from the control (based on Bonferroni T-test results using TOXSTAT v3.0). The reductions in body weight increase led to a determination of an 8-day NOAEC of 1780 mg a.i./kg-diet for the duck study. This NOAEC is based on the total change in body weight from day 0 to day 8. The APVMA primary reviewer calculated the 5-day NOAEC instead and determined it to be 1000 mg a.i./kg-diet. The use of one or the other will depend on physico-chemical properties and use of pyroxasulfone. For example, if pyroxasulfone is short lived and used infrequently then the 0-8 day value would be more applicable; however, if the chemical is more stable and/or used frequently then an interest in transient weight loss during exposure would vindicate the use of the 0-5 day value as exposure in the field would be expected to be higher longer. Given the stability of pyroxasulfone the latter statement and the 1000 mg a.i./kg-diet value would apply. The duck study indicated no mortalities, overt signs of toxicity, or treatment-related effects on food consumption at the dosage levels tested.

Bird – Metabolites/Degradates

There are no acute data on metabolites/degradates for birds.

Bird – Formulations

There are no acute data on formulations for birds, as these data are not required.

Table 28. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50}/LC_{50} NOAEL/ LOAEL**	**MRID**	**Classification /Category**
Technical KIH-485					
Northern Bobwhite Quail *Colinus virginianus*	99.1	Acute oral study 1 replicate of 5♂ and 5♀ birds per treatment group and control (10 birds/treatment and control; 2 pens per treatment and control group with 5 birds of one sex per pen) 14 day observation period Nominal: negative control, 292, 486, 810, 1350, and 2250 mg a.i./kg-bw	14-day LD_{50} > **2250**[3] mg a.i./kg bw 14-day NOAEL ≥ 2250 mg a.i./kg bw Endpoint(s) affected: None. *Sublethal effects*: None.	47701631	Acceptable/ Practically non-toxic[1]
Zebra finch *Poephila guttata*	98.82	Acute oral study (limit test) 1 replicate of 5♂ and 5♀ birds per treatment group and control (10 birds/treatment and control); birds were housed in pairs 14 day observation period Nominal: negative control, 2250 mg a.i./kg-bw	14-day LD_{50} > 2250 mg a.i./kg bw 14-day NOAEL ≥ 2250 mg a.i./kg bw Endpoint(s) affected: None. *Sublethal effects*: None.	47701632	Acceptable/ Practically non-toxic[1]

Table 28. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50}/LC_{50} NOAEL/ LOAEL**	**MRID**	**Classification /Category**
Northern Bobwhite Quail *Colinus virginianus*	99.1	Acute <u>dietary</u> study 3 in control (30 birds total; 6 pens with 5 birds/pen); 1 in treatment (10 birds/treatment; 2 pens with 5 birds of undetermined sex/pen) 5-day exposure period, 3 additional days observation with untreated basal diet Nominal: negative control, 562, 1000, 1780, 3160, and 5620 mg a.i./kg-diet	8-day LC_{50} >**5620**[3] mg a.i./kg diet 8-day NOAEC $\geq$ 5620 mg a.i./kg diet Endpoint(s) affected: None. *Sublethal effects*: A couple of control birds were observed with leg lesions and were limping. Similarly, one bird in each of the 1780 mg a.i./L and 5620 mg a.i./L treatment groups was observed limping. The bird in the 5620 mg a.i./L treatment group also exhibited wing droop. Likely due to pen-mate aggression and not treatment related.	47701633	Acceptable/ Practically non-toxic[2]
Mallard Duck *Anas platyrhynchos*	99.1	Acute <u>dietary</u> study 3 in control (30 birds total; 6 pens with 5 birds/pen); 1 in treatment (10 birds/treatment; 2 pens with 5 birds of undetermined sex/pen) 5-day exposure period, 3 additional days observation with untreated basal diet Nominal: negative control, 562, 1000, 1780, 3160, and 5620 mg a.i./kg-diet	8-day LC_{50} > 5620 mg a.i./kg diet 8-day NOAEC: 1780 mg a.i./kg diet* Endpoint(s) affected: body weight increase *Sublethal effects:* change in body weight. **NOAEC is based on the total change in body weight from day 0 to day 8. The APVMA primary reviewer calculated the <u>5-day NOAEC as 1000 mg a.i./kg-diet</u>. The use of one or the other will depend on physico-chemical properties and use of pyroxasulfone: if short lived and used infrequently then the 0-8 day value would be more applicable; however, if the chemical is more stable and/or used frequently then an interest in transient weight loss during exposure would vindicate the use of the 0-5 day value as exposure in the field would be expected to be higher longer.*	47701634	Acceptable/ Practically non-toxic[2]

Table 28. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50}/LC_{50} NOAEL/ LOAEL**	**MRID**	**Classification /Category**
[1] Based on LD_{50} (mg/kg) <10 very highly toxic; 10-50 highly toxic; 51-500 moderately toxic; 501-2000 slightly toxic; >2000 practically nontoxic [2] Based on LC_{50} (mg/kg) <50 very highly toxic; 50-500 highly toxic; 501-1000 moderately toxic; 1001-5000 slightly toxic; >5000 practically nontoxic [3]**Bold** value used in risk description					

Mammals - Technical and degradate/metabolite

Eight acute oral studies were conducted on female rats to satisfy OCSPP guidance 870.1100 (OECD 425) – one technical and seven degradate/metabolite (M-1, M-3, M-25, I-3, I-4, I-5, M-28). All of the studies were deemed acceptable and indicated that the test compound was practically non-toxic with toxicity category III. However, all of the studies were conducted at a limit dose of 2000 mg a.i./kg-bw and without control groups.

Mammals – Formulations

Two formulation studies were conducted on female rats to satisfy OCSPP guidance 870.1100 (OECD 425) – one on WG85 (85%a.i.) and one on V-10233 (42.2% pyroxasulfone; 33.6 flumioxazin). Both studies were limit tests and deemed acceptable; however, no control groups were used in the study design. The single active ingredient product tested (MRID 47701916) is at most slightly toxic (category III), while the co-formulated product (MRID 47702105) is practically non-toxic (category IV) at the respective limit doses. No deaths or sublethal effects were observed in either study.

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Technical KIH-485					
Rat, IGSBR strain (♀ only)	99.1	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in 0.5% aqueous sodium carboxymethylcellulose with Tween 80 (60:1) administered by gavage 2 groups of 3 rats (9wks old; 172-195g) 15-day observation period	Acute oral LD_{50} ♀>**2000**[2] mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* None. No deaths or clinical signs. All rats gained weight during the first and second weeks of obs. period except for one animal which showed a slight loss in body weight during the second week.	47701677	Acceptable/ Practically non-toxic[1] Toxicity category III

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Metabolites/Degradates					
Rat, IGSBR strain (♀ only)	99.95% M-1	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in distilled water administered by gavage 2 groups of 3 rats (8-12 wks old; 186-206g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* No deaths. Systemic toxicity signs included hunched posture, lethargy, pilo-erection, decreased respiratory rate, tiptoe gait. One animal appeared normal throughout test; remaining animals appeared normal 2-6 days after dosing.	47701678	Acceptable/ Practically non-toxic[1] Toxicity category III
Rat, IGSBR strain (♀ only)	100% M-3	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in arachis oil BP (b/c test matl. did not dissolve in distilled water) administered by gavage 2 groups of 3 rats (8-12 wks old; 194-219g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* No deaths. Hunched posture obs in all animals. Animals appeared normal 1-3 days after dosing.	47701679	Acceptable/ Practically non-toxic[1] Toxicity category III

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Rat, SPF strain (♀ only)	98.72% M-25	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in purified water administered by gavage 2 groups of 3 rats (11 wks old; 180.8-196.5g) 15-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* No deaths. 3/6 rats did not show any clinical signs throughout test. Two hours post-dosing, a slightly ruffled fur was observed in 3 females which persisted up to the 5-hour observation. Slight sedation was observed in two rats 2-5 hrs after treatment. Hunched posture and slightly poor coordination obs in 3 rats during the same observation period. Additionally, one rat was observed with shut eyes 2-5 hours post-dose. The 3 rats were free of clinical signs from test day 2-15.	47701680	Acceptable/ Practically non-toxic[1] Toxicity category III
Rat, IGSBR strain (♀ only)	96.59% I-3	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in dimethyl sulphoxide (b/c test matl. did not dissolve in distilled water or arachis oil BP) administered by gavage 5 rats treated at given dose level (8-12 wks old; 211-256 g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* No deaths. Increased salivation obs in one rat.	47701681	Acceptable/ Practically non-toxic[1] Toxicity category III

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Rat, IGSBR strain (♀ only)	96.86% I-4	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in dimethyl sulphoxide (b/c test matl. did not dissolve in distilled water or arachis oil BP) administered by gavage 5 rats treated at given dose level (8-12 wks old; 207-268 g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* No deaths. Hunched posture and ataxia were noted during the day of dosing in 2 rats.	47701682	Acceptable/ Practically non-toxic[1] Toxicity category III
Rat, IGSBR strain (♀ only)	99.95% I-5	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in dimethyl sulphoxide (b/c test matl. did not dissolve in distilled water or arachis oil BP) administered by gavage 5 rats treated at given dose level (8-12 wks old; 208-258 g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* None.	47701683	Acceptable/ Practically non-toxic[1] Toxicity category III

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Rat, IGSBR strain (♀ only)	99.65% M-28	Acute oral study Dose level: 2000 mg a.i./kg bw (limit test) – i.e., a.i. mixed in purified water administered by gavage 2 groups of 3 rats (8-12 wks old; 192-233 g) 14-day observation period	Acute oral LD_{50} ♀>2000 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:* 2 deaths. Piloerection, salivation, underactivity, reduced body tone, hunched posture, and body weight loss prior to death. Darkened tissues of lungs, kidneys, liver obs after death. Piloerection, underactivity, unsteady gait, and reduced body temp obs in remaining rats but resolved by day 4.	47701755	Acceptable/ Practically non-toxic[1] Toxicity category III
Formulations					
Rat, SPF strain (♀ only)	85% WG85	Acute oral study Dose level 1,700 mg a.i./kg-bw (limit test: 2000 mg form/kg-bw) – i.e. mixed in purified water administered by gavage 2 groups of 3 rats (11 wks old; 177.2-193.6 g) 15-day observation period	Acute oral LD_{50} ♀> 1,700 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:*None.	47701916	Acceptable/ At most, slightly toxic[1] Toxicity category III

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Rat, Sprague-Dawley (♀ only)	42.2% pyroxasulfone; 33.6 flumioxazin V-10233 (VC1763)	Acute oral study Dose level 2,110 mg a.i./kg-bw (limit test: 5000 mg form/kg-bw) – i.e. mixed in 50% w/w distilled water administered by gavage 1 group of 3 rats (11 wks old; 190-215g) 14-day observation period	Acute oral LD_{50} ♀>2,110 mg a.i./kg bw NOAEL: No NOAEL LOAEL: No LOAEL Endpoint(s) affected: None. *(Sub)lethal effects:*None.	47702105	Acceptable / Practically non-toxic[1] Toxicity category IV
Inhalation studies (870.1300) for STIR – Technical and formulations					
Rat, IGSBR strain	99.1 (TGAI)	Acute inhalation toxicity (limit test) Atmospheric concentration of 6.56 mg/L (MMAD = 4.18 µm; GSD = 1.91) Exposed by inhalation (nose only) route; 5♂ & 5♀ (8 wks old; ♂: 243-278 g; ♀: 182-210 g) 4-hour (4 hours and 29 minutes) exposure period; observed for 15 days	LC_{50} ♂ > 6.56 mg a.i./L LC_{50} ♀ > 6.56 mg a.i./L LC_{50} Combined > **6.56**[3] mg a.i./L Endpoint(s) affected: None. *(Sub)lethal effects*: During exposure effects to breathing pattern and tail pinch reflex were observed. After exposure effects included hunched posture, piloerection, stained fur, and nasal discharge.	47701685	Acceptable / Toxicity Category IV

Table 29. Mammalian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification/ Category**
Rat, albino SPF strain	85 (WG 85)	Acute inhalation toxicity (limit test) Analytically determined mean concentration of 5.8 mg form/L (MMAD = 3.45-3.62 µm; GSD = 2.73-3.62); 4.93 mg a.i./L Exposed by inhalation (nose only flow past) route; 5♂ & 5♀ (8 wks old; ♂: 256.2-276.2 g; ♀: 171.4-181.8 g) 4-hour exposure period; observed for 15 days	LC_{50} ♂ > 4.93 mg a.i./L LC_{50} ♀ > 4.93 mg a.i./L LC_{50} Combined > 4.93 mg a.i./L Endpoint(s) affected: None. *(Sub)lethal effects*: None.	47701918	Acceptable / Toxicity Category IV
Rat, albino Sprague-Dawley	42.2% pyroxasulfone; 33.6 flumioxazin V-10233 (VC1763)	Acute inhalation toxicity (limit test) Gravimetric concentration of 2.04 mg form/L (MMAD = 3.6 µm; GSD = 1.99); 0.86 mg a.i./L Exposed by inhalation (nose only flow past) route; 5♂ & 5♀ (10-11 wks old; ♂: 333-367 g; ♀: 215-247 g) 4-hour exposure period; observed for 14 days	LC_{50} ♂ > 0.86 mg a.i./L LC_{50} ♀ > 0.86 mg a.i./L LC_{50} Combined > 0.86 mg a.i./L Endpoint(s) affected: None. *(Sub)lethal effects*: None.	47702107	Acceptable / Toxicity Category IV

[1] Based on LD_{50} (mg/kg) <10 very highly toxic; 10-50 highly toxic; 51-500 moderately toxic; 501-2000 slightly toxic; >2000 practically nontoxic
[2]**Bold** value used in risk description
[3]**Bold** value used in STIR; though the formulation studies indicate lower concentrations on a %a.i. basis, the TGAI study had an indication of sublethal effects (though apparently transient).

Terrestrial Invertebrates – Technical

The terrestrial invertebrate study on honey bees (*Apis mellifera*, MRID 47701637) is classified as acceptable. The acute contact test cumulative mortality over the 48 hour testing period for the negative control, solvent control (acetone), and nominal test concentrations 1.94, 4.27, 9.4, 20.7, 45.5, and 100 µg a.i./bee was 11.7, 3.3, 21.7, 10, 6.7, 15, 15, and 10% , respectively. As a result, the 48-hour LD_{50} > 100 µg a.i./bee (the highest concentration tested). For the positive control (dimethoate) nominal test concentrations 0.05, 0.1, and 0.3 µg a.i./bee, cumulative mortality was 8.3, 11.7, and 100%. Sub-lethal effects were sporadic and apparently not treatment-related, but include lethargy, loss of equilibrium, and immobility. More specifically, there were sporadic occurrences of lethargy (two cases during the first half hour in the 9.4 and 100 µg a.i./L concentration; one case at 1.5 hours in the 100 µg a.i./L concentration), loss of equilibrium (one case after 24 hours in the 20.7 µg a.i./L concentration), and immobility (three cases after 48 hours: one in the 1.94 µg a.i./L concentration and two in the 4.27 µg a.i./L concentration).

Non-guideline studies – Technical and Formulations
A terrestrial invertebrate study on parasitoid wasp (*Aphidius rhopalosiphi*, MRID 47889323) using the pyroxasulfone proposed formulation WG85 (84.7% purity) is classified as supplemental by the Agency on account of being a non-guideline study. The review and toxicity calculations were performed by APVMA; the study received a 'fully reliable' rating. There were no mortalities or toxic effects in the control or any of the treatment groups. William's test was used to calculate effects on fecundity which showed a significant decrease in the reproduction parameter (*i.e.,* mean number of parasitized aphids per female) at the two highest test concentrations. However, the primary reviewer noted that the application of KIH-485 (pyroxasulfone) WG85 to the parasitoid wasp resulted in up to 45% reduction in fecundity. As 50% reduction in fecundity was not reached at any level of exposure to pyroxasulfone, an ER_{50} was not calculated from the data available and was thus considered as greater than the highest concentration tested (*i.e.*, >1000 g a.i./ha).

A terrestrial invertebrate study on predatory mite (*Typhlodromus pyri*, MRID 47701753) using the pyroxasulfone proposed formulation WG85 (84.7% purity) is classified by the Agency as supplemental on account of being a non-guideline study. The review and toxicity calculations were performed by APVMA; the study was considered valid and received a 'fully reliable' rating. Fisher's exact test was used to assess mortality and Williams test to assess fecundity (*i.e.*, eggs produced per female per day). Mite mortality in the water control reached 3% within 7 days of exposure. Corrected mortality for KIH-485 (pyroxasulfone) WG85 applied at rates of 62.5, 125, 250, 500 and 1000 g a.i./ha was 6, 6, 8, 3 and 8% respectively within 7 days. Positive control (dimethoate) mortality was 94% by seven days. The 7-day LR_{50} was > 1000 g a.i./ha. There were statistically significant reductions in fecundity in all the KIH-485 (pyroxasulfone) WG85 treated groups compared to the control group. The application of KIH-485 (pyroxasulfone) WG85 resulted in up to 50% reduction in total beneficial effect (*i.e.*, E = 100% - (100% - Ma) × Er), where Ma is corrected mortality and Er is the proportional difference in reproduction) of predatory mites. However, the response was not dose dependent. Therefore, based on nominal concentration, the 7-day LR_{50} of KIH-485 (pyroxasulfone) WG85 to *Typhlodromus pyri* was >1000 g a.i./ha.

A terrestrial invertebrate study on earthworm (*Eisenia fetida*, MRID 47701748) using the pyroxasulfone technical (98.82% purity) is classified by the Agency as supplemental on account of being a non-guideline study. The review and toxicity calculations were performed by APVMA; the study received a 'fully reliable' rating. There were no mortalities in the control group or any of the treatment groups during the 14-day test. The average total weight change in the control was -0.11 ± 0.013 g (SD) and -0.14 ± 0.017 g in the highest treatment group. The weight loss did not appear to be dose responsive. Treatment-related effects were not observed in the test. All earthworms in the control group and treatment groups were normal in appearance and behavior throughout the test period. Earthworms in both the control and treatment groups exhibited no aversion to the soil during observations of burrowing behavior on Days 0 and 7. The LC_{50} and NOAEC were determined by visual examination of the mortality and clinical observation data.

A terrestrial invertebrate study on earthworm (*E. fetida*, MRID 47933801) testing growth and reproduction and using the pyroxasulfone technical (99.21% purity) is classified by the Agency as supplemental on account of being a non-guideline study. The review and toxicity calculations were performed by APVMA; the study received a 'fully reliable' rating. There were no adult mortalities in any of the treatments or controls. Adult bodyweight increases were similar in treated groups to the control. Production of juveniles was similar in each group. Under the conditions of this study it can be concluded that reproductive performance in *E. fetida* was unaffected by pyroxasulfone at soil concentrations of up to 1000 ppm (presumably mg a.i./kg dry soil).

Table 30. Terrestrial Invertebrate Acute Toxicity Data

Common Name	%AI	Study parameters	LD_{50} /NOAEL	MRID	Classification /Category
Technical KIH-485					
Honey bees *Apis Mellifera*	99.1	48-hour acute contact 3 reps.; 20 bees per rep.; 60 bees per treatment Nominal: negative control, solvent control (acetone), 1.94, 4.27, 9.4, 20.7, 45.5, and 100 µg a.i./bee; for positive control (dimethoate): 0.05, 0.1, and 0.3 µg a.i./bee	48 hour LD_{50} > **100**[2] µg ai/bee NOAEC: 100 µg a.i./bee LOAEC > 100 µg a.i./bee Endpoint(s) affected: None. Endpoint(s) considered: mortality. *Sublethal effects:* Sporadic and apparently not treatment-related, but include lethargy, loss of equilibrium, and immobility.	47701637	Acceptable/ Practically non-toxic[1]
Non-guideline studies – Technical and Formulation					

Table 30. Terrestrial Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification /Category**
Parasitoid wasp *Aphidius rhopalosiphi*	Formulation WG85 (84.7%)	48 hour exposure period; parasitized aphids counted on day 11 4 reps (of 5♀: 5♂) / 40 bees per treatment Nominal: 0 (water control), 12.35, 37.04, 111.11, 333.33, and 1000 g a.i./ha; 0, 0.011, 0.033, 0.099, 0.297, and 0.892 lbs a.i./A	48-hour ER_{50} / LR_{50}[4] > 1000 g a.i./ha (equivalent to >0.892 lbs a.i.A) Endpoint(s) affected: fecundity (parasitization of aphids) Endpoint(s) considered: mortality, fecundity *Sublethal effects*: No toxic effects recorded in control or treatment groups.	47889323	Supplemental[3]
Predatory mite *Typhlodromus pyri*	Formulation WG85 (84.7%)	7-day exposure period; endpoints also assessed on day 9, 11, and 14 5 reps (of 20mites) / 100 mites per treatment Nominal: 0 (water control), 62.5, 125, 250, 500, and 1000 g a.i./ha; 0, 0.056, 0.112, 0.223, 0.446, and 0.892 lbs a.i./A	7-day ER_{50} / LR_{50}[4] > 1000 g a.i./ha (equivalent to >0.892 lbs a.i.A) Endpoint(s) affected: mortality, fecundity (overall eggs per female per day) Endpoint(s) considered: mortality, fecundity *Sublethal effects*: No toxic effects recorded in control or treatment groups.	47701753	Supplemental[3]
Earthworm *Eisenia fetida*	98.82	14-day exposure period (in artificial soil) 4 reps (of 10 earthworms) / 40 earthworms per treatment Nominal: 0, 62.3, 125, 249, 499, and 997 mg a.i./kg dry soil	14-day LC_{50} > 997 mg a.i./kg dry soil 14-day NOAEC: 997 mg a.i./kg dry soil Endpoint(s) affected: None. Endpoint(s) considered: mortality, bodywt loss *Sublethal effects*: None.	47701748	Supplemental[3]

Table 30. Terrestrial Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**LD_{50} /NOAEL**	**MRID**	**Classification /Category**
Earthworm *Eisenia fetida*	99.21	4 week exposure period of adults; 2nd 4-wk obs pd for juvenile worms; reproduction and growth study 4 reps (of 10 earthworms) / 40 earthworms per treatment Nominal: 0, 1.6, 8.0, 40, 200 and 1000 ppm	28-day NOAEC ≥ 1000 ppm[5] Endpoint(s) affected: None. Endpoint(s) considered: mortality, bodywt loss, juvenile counts *Sublethal effects*: None.	47933801	Supplemental[3]

[1] Based on acute contact LD_{50} (μg a.i./bee) <2 highly toxic; 2-10.99 moderately toxic; ≥11 practically non-toxic
[2] **Bold** value used in risk description
[3] Supplemental on account of being a non-guideline study.
[4] ER_{50}: effect level corresponds to fecundity calculation; LR_{50}: lethal level corresponds to mortality calculation
[5] Presumed to refer to following units: mg a.i./kg dry soil

(2) Chronic Effects

Birds - Technical

The one-generation reproductive toxicity study (MRID 47701635) using 16 pairs per level of 34-week old Northern bobwhite quail (*Colinus virginianus*) over 20 weeks was classified as acceptable. KIH-485 technical was administered to the birds in the diet at nominal concentrations of 0 (control), 100, 300, 1000 mg a.i./kg-diet. Mean-measured concentrations were <25 (control), 97.1, 295.5, 1004.5 mg a.i./kg-diet, respectively. There were no apparent treatment-related effects upon adult body weight, reproductive performance, eggshell thickness, or offspring body weight at any of the concentrations tested. The lack of dose response in this case indicates that the NOAEC ≥ 1,000 mg a.i./kg diet and LOAEC will be > 1,000 mg a.i./kg diet. As the endpoints are non-definitive, they are not useful for RQ calculations, but can contribute to risk description.

The one-generation reproductive toxicity study (MRID 47701636) used 16 pairs per level of *ca.* 24-week old mallard duck (*Anas platyrhynchos*) over 20 weeks was classified as acceptable. KIH-485 technical was administered to the birds in the diet at nominal concentrations of 0 (control), 60, 240, and 600 mg a.i./kg-diet. Mean-measured concentrations were <25 (control), 60.9, 243, and 621.5 mg a.i./kg-diet, respectively. At the 600 mg a.i./kg-diet nominal test concentration, there was a slight, treatment related decrease in adult body weight during the period from week 4 to week 8. There were no apparent treatment related effects on egg shell thickness at any concentration tested. At the 600 mg a.i./kg-diet nominal test concentration, there were treatment-related decreases in body weight of both hatchling and 14-day old survivors that were statistically significant. For the nominal concentrations 0, 60, 240, and 600 mg a.i./kg-diet, the total number of eggs set is 620, 534, 553, and 381, respectively. When hatchability, with respect to the number of hatchlings hatched out of the number of eggs set, above 70% per pair was considered, it was found that in the control group, hatchability was above 70% in 9 of 15 pairs (*i.e.*, those alive and with hatchlings; a total of 16 pairs were used in the study), while in the 240 and 600 mg a.i./kg-diet treatment group only 2 of 13 pairs were above 70%; the 60 mg a.i./kg-diet was comparable to the control with 7 of 12 pairs above 70%. Furthermore, according to OCSPP guidance 850.2300, normal values for hatchability for mallards are between 50 and 90%; when hatchability above 50% per pair was considered, it was found that in the control group, hatchability was at or above 50% in 11 of the 15 pairs (*i.e.*, those alive and with hatchlings), while in the 240 and 600 mg a.i./kg-diet treatment groups only 2 and 5, respectively, out of 13 pairs were above 50%; the 60 mg a.i./kg-diet was again comparable to the control with 10 of 12 pairs above 50%. The means (standard deviation) for hatchability across the control and three test concentrations are 59% (25), 74% (19), 39% (21), and 28% (27), which includes pairs for which eggs were set but not hatched – this makes for 16 pairs in the control, 12, 14, and 14 in the respective concentrations. As a result, there appears to be a dose-dependent effect on hatchability. Therefore, on a biological significance basis, the NOAEC was determined to be 60 mg a.i./kg-diet and the LOAEC 240 mg a.i./kg-diet.

Bird – Metabolites/Degradates
There are no chronic data on metabolites/degradates for birds.

Bird – Formulations
There are no chronic data on formulations for birds, as these data are not required.

Table 31. Avian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**NOAEC/LOAEC**	**MRID**	**Classification**
Technical KIH-485					
Northern Bobwhite Quail *Colinus virginianus*	99.1	1-generation reproduction study Dietary study 20 weeks 2 birds per pen (1 ♂: 1♀); 16 pens per neg. control and treatment Nominal: Negative control, 100, 300, 1000 mg a.i./kg-diet Mean measured: Negative control (<25), 97.1, 295.5, 1004.5 mg a.i./kg-diet (based on week 1 results)	NOAEC ≥ 1000 mg a.i./kg diet LOAEC > 1000 mg a.i./kg diet Endpoint(s) affected: none. *Mortality*: Three incidental mortalities occurred during the test, two in the 100 mg a.i./kg-diet and one in the 300 mg a.i./kg-diet treatment group, but were not considered treatment related. *Sublethal effects*: Clinical observations indicated incidental injuries not atypical for penwear such as feather loss, lesions (feet, legs, head, back or wings), lameness, loss of coordination, and ruffled appearance. Necropsy findings were apparently not attributed to treatment.	47701635	Acceptable

Table 31. Avian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**NOAEC/LOAEC**	**MRID**	**Classification**
Mallard Duck *Anas platyrhynchos*	99.1	1-generation reproduction study Dietary study 20 weeks 2 birds per pen (1 ♂: 1♀); 16 pens per neg. control and treatment Nominal: Negative control, 60, 240, and 600 mg a.i./kg-diet Mean measured: Negative control (<25), 60.9, 243, and 621.5 mg a.i./kg-diet	NOAEC: **60**[1] mg a.i./kg diet LOAEC: 240 mg a.i./kg diet Endpoint(s) affected: reproductive performance (hatchability) *Mortality*: Single incidental mortalities occurred during the test in both the 60 and 600 mg a.i./kg-diet treatment groups, but were not considered treatment related. *Sublethal effects:* Clinical observations indicated incidental injuries not atypical for penwear such as feather loss, swollen sinus, swelling around the eye, foot lesions, lameness, and reduced reaction to external stimuli. Necropsy findings were apparently not attributed to treatment.	47701636	Acceptable
[1]**Bold** value used in risk quotient calculation					

Mammals - Technical

A non-guideline 1-generation rat reproduction study (MRID 47701705) was classified as acceptable. The LOAEL for parental (P) toxicity is 5000 mg a.i./kg-diet (equivalent to 339/383 mg/kg-bw/day in males/females, respectively) based on microscopic effects in the heart, liver, muscle, and sciatic nerve of males and females, decreased body weight gains in the P males and females and decreased food efficiency in the P dams. The NOAEL for parental toxicity is 250 mg a.i./kg-diet (equivalent to 16/20 mg/kg-bw/day in males/females, respectively). The LOAEL for offspring toxicity is 5000 mg a.i./kg-diet (equivalent to 339/383 mg/kg-bw/day in males/females, respectively) based on decreased body weight gains in the P males and females and decreased food efficiency in the P dams. The NOAEL for offspring toxicity is 250 mg a.i./kg-diet (equivalent to 16.0/19.6 mg/kg-bw/day in males/females, respectively). The LOAEL for reproductive toxicity was not observed. The NOAEL for reproductive toxicity is 5000 mg a.i./kg-diet (equivalent to 339/383 mg/kg-bw/day in males/females, respectively), the highest concentration tested.

A rat 2-generation reproduction study (MRID 47701706) was classified as acceptable. The LOAEL for parental toxicity is 2000 mg a.i./kg-diet (equivalent to 144/165 mg/kg-bw/day in males/females, respectively) based on decreased body weights, body weight gains, and food consumption. The NOAEL is 100 mg a.i./kg-diet (equivalent to 7.2/8.4 mg/kg-bw/day in males/females, respectively). The LOAEL for offspring toxicity is 2000 mg a.i./kg-diet (equivalent to 144/165 mg/kg-bw/day in males/females, respectively) based on decreased pup body weights and body weight gains. The NOAEL is 100 mg a.i./kg-diet (equivalent to 7.2/8.4 mg/kg-bw/day in males/females, respectively). The LOAEL for reproductive toxicity was not observed. The NOAEL for reproductive toxicity is 2000 mg a.i./kg-diet (equivalent to 144/165 mg/kg-bw/day in males/females, respectively), the highest dose tested.

A rat developmental toxicity study (MRID 47701702) was classified as acceptable. The maternal and developmental LOAELs were not observed. The maternal and developmental NOAELs are 1000 mg/kg/day (limit dose).

A rabbit developmental toxicity study (MRID 47701704) was classified as acceptable. The LOAEL for maternal toxicity was not observed. The NOAEL for maternal toxicity is 1000 mg/kg/day (limit dose). The LOAEL for developmental toxicity is 1000 mg/kg/day (limit dose) based on reduced fetal weight and increased fetal resorptions. The NOAEL for developmental toxicity is 500 mg/kg/day.

Table 32. Mammalian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**NOAEC/ LOAEC**	**MRID**	**Classification/ Category**
Technical KIH-485					
Rat, IGS BR strain	97.2	1-generation reproduction study 12 CD Sprague-Dawley rats/sex/concentration, **by feeding (diet)**; fed for ≥28 days prior to mating (P generation) 3 treatment groups; 1 untreated diet control group Nominal: 0, 25, 250, 5000 ppm	Parental toxicity NOAEL[2] (M/F): 16/20 mg/kg bw/day LOAEL[3] (M/F): 339/383 (HDT) mg/kg bw/day Offspring Toxicity NOAEL (M/F): 16/19.6 mg/kg bw/day LOAEL (M/F): 339/383 (HDT) mg/kg bw/day[4] Reproductive Toxicity NOAEL (M/F): 339/383 mg/kg bw/day LOAEL (M/F): not attained	47701705	Acceptable / Non-Guideline [*] Provides data for use in dose selection for definitive 2-generation reproductive toxicity study in rats
Rat, IGS BR strain	99.1	2-generation reproduction study 30 CD Sprague-Dawley rats/sex/concentration, **by feeding (diet)**; fed test diets for 10 wks prior to mating (P and F1 generations) 3 treatment groups; 1 untreated diet control group Nominal: 0, 5, **100**[1], 2000 ppm ♂:0, 0.4, 7.2, 144 mg/kg-bw/day ♀: 0, 0.4, 8.4, 165 mg/kg-bw/day	Parental toxicity NOAEL (M/F): **7.2**[1]/8.4 mg/kg bw/day LOAEL[5] (M/F): 144/165 mg/kg bw/day Offspring Toxicity NOAEL (M/F): 7.2/8.4 mg/kg bw/day LOAEL[6] (M/F): 144/165 mg/kg bw/day Reproductive Toxicity NOAEL (M/F): 144/165 mg/kg bw/day LOAEL (M/F): not attained	47701706	Acceptable / Guideline

Table 32. Mammalian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**NOAEC/ LOAEC**	**MRID**	**Classification/ Category**
Rat (time-mated ♀ only)	99.1	Developmental toxicity study 22 CD Sprague-Dawley rats per dose, **by gavage**. 3 treatment groups; 1 untreated control group 0, 100, 500, 1000 mg a.i./kg bw/day	*Maternal* NOAEL: 1000 mg/kg/day LOAEL: not attained *Developmental* NOAEL: 1000 mg/kg/day LOAEL: not attained	47701702	Acceptable/ Guideline
Rabbit (time-mated ♀ only)	99.1	Developmental toxicity study 22 Hra: (NZW) SP rabbits per group, **by gavage**. 3 treatment groups; 1 untreated control group 0, 250, 500, 1000 mg a.i./kg-bw/day	*Maternal*[7] NOAEL: 1000 mg a.i./kg-bw/day LOAEL: not attained *Developmental* NOAEL: 500 mg a.i./kg-bw/day LOAEL[8]: 1000 mg a.i./kg-bw/day	47701704	Acceptable/ Guideline

[1] **Bold** value is the value that will be used to calculate risk quotients
[2] Decreased body wt gains at the 250 ppm (*i.e.*, 16/20 mg/kg bw/day) dose were transient and mostly not statistically significant; but body wts were not affected. Therefore, effects at 250 ppm are equivocal.
[3] Based on microscopic effects in the heart, liver, muscle, and sciatic nerve in males and females, body wt gain in P males and females, and decreased food efficiency in P dams.
[4]Based on decreased pup wt and delayed sexual maturation in both sexes
[5]Based on decreased body wt, body wt gain, and food consumption
[6]Based on decreased pup body wts and body wt gains.
[7]Seven females died or were euthanized prior to scheduled necropsy, 3 due to premature abortion and 4 because of intubation injury. One abortion occurred at 250 mg a.i./kg-bw/day and two occurred at 1000 mg a.i./kg-bw/day. However, there were no test-substance related deaths or sublethal effects in dams at any level tested.
[8]Based on reduced fetal weight and increased fetal resorptions (total and early) at 1000 mg a.i./kg-bw/day

b. Terrestrial Plants

The seedling emergence study (MRID 47701638) is classified as supplemental because it is scientifically sound but does not satisfy the data requirement for a Tier II seedling emergence toxicity study. The study was intended to identify a ≥25% effect on emergence, survival, height, and dry weight for 10 species of plants. A most sensitive monocot and dicot were identified. However, some of the data indicate ≥25% effect at higher concentrations that are not statistically significant. For example, sunflower (dicot) had a 23 and 52% increase in dry weight at the two highest concentrations (0.1338 and 0.2676 lbs a.i./A) that were not detected as statistically significant. Furthermore, wheat (monocot) dry weight (MSD 41.21%) had the following percent reductions 22, 22, 12, 2.5, and 28% relative to the control which were not detected as statistically significant at 0.0168, 0.0334, 0.0669, 0.1338, and 0.2676 lbs a.i./A concentrations, respectively. This indicates that the study may not capture what it was intended to capture as there was high variability in the raw data. For wheat, this implies that sublethal effects may be observed below maximum application levels and below the lowest tested concentration. The most sensitive monocot was the onion (*Allium cepa*) with an EC_{25} of 0.0669 lbs a.i./A and NOAEC of 0.0168 lbs a.i./A based on the observed changes in length. However, the significant effect on survival (3, 33, 12, 6, 27 and 42% relative to the control at 0.00418, 0.00837, 0.0168, 0.0334, 0.0669 and 0.1338 lbs a.i./A, respectively; MSD of 28%) may have confounded the results for the length parameter. The most sensitive dicot was the kidney bean (*Phaseolus vulgaris*) with an EC_{25} of 0.2615 lbs a.i./A (just below the highest concentration tested – i.e., 0.2676 lbs a.i./A) and NOAEC of 0.1338 lbs a.i./A based on observed changes in length.

The vegetative vigor study (MRID 47701639), however, is classified as acceptable because it is scientifically sound and satisfies the data requirement for a Tier II vegetative vigor toxicity study. Monocots, overall, did not exhibit signs of treatment-related toxicity, whereas dicots did. However, there is some uncertainty in these results considering that potential weeds or pest species are monocots (e.g., barnyard millet, Italian ryegrass). As a result determining the most sensitive monocot (*i.e.*, onion *A. cepa*) was based on the lowest EC_{25} of the monocots for which the endpoint was available. However, the EC_x's for onion (as well as most monocot data) did not indicate convergence whereby an algorithm was not plotted against the data indicating clear inhibition with increasing concentration. As a result, for onion the $EC_{25} > 0.2676$ lbs a.i./A (the highest concentration tested) and the NOAEC is equal to the highest concentration tested. On the other hand, the most sensitive dicot was the pumpkin (*Cucurbita mixta*) with an EC_{25} of 0.0748 lbs a.i./A and NOAEC of 0.0168 lbs a.i.A.

Table 33. Terrestrial Plant Toxicity Data					
Study Type	**%AI**	**Study Parameters**	**EC_{05}/EC_{25}/NOAEC**	**MRID**	**Classification**
KIH-485 TEP					
Seedling Emergence – Tier II	85	21 days 4 reps per test group; 10 seeds per rep. Concentrations tested: negative control, 9.38, 18.8, 37.5, 75, 150, 300 g a.i./ha (for *R. sativa*) negative control, 4.69, 9.38, 18.8, 37.5, 75, 150 g a.i./ha (for *A. cepa)* negative control, 18.8, 37.5, 75, 150, 300 g a.i./ha (for all others) [Concentrations in lbs a.i./A (from lowest to highest tested): 0.0048, 0.00837, 0.0168, 0.0334, 0.0669, 0.1338, 0.2676 lbs a.i./A]	<u>Most sensitive dicot</u> Kidney bean (*Phaseolus vulgaris*; Fabaceae) – length EC_{05}: 0.1044 (0.024-0.45) lbs a.i./A **EC_{25}: 0.2615 (0.17-0.41) lbs a.i./A** EC_{50}: 0.4950 (0.17-1.46) lbs a.i./A **NOAEC: 0.1338 lbs a.i./A** <u>Most sensitive monocot</u> Onion (*Allium cepa*; Liliaceae) – length EC_{05}: 0.0048 (0.0003-0.08) lbs a.i./A **EC_{25}: 0.0669 (0.02-0.19) lbs a.i./A** EC_{50}: 0.4164 (0.12-1.46) lbs a.i./A **NOAEC: 0.0168 lbs a.i./A** Endpoints affected: length (or height), dry weight *Sublethal effects:* Incidental observations of chlorosis, necrosis, stem curl, leaf curl. Typically, the effects were observed at or above the LOAEC for height or weight.	47701638	Supplemental

Table 33. Terrestrial Plant Toxicity Data					
Study Type	**%AI**	**Study Parameters**	**EC_{05}/EC_{25}/NOAEC**	**MRID**	**Classification**
Vegetative Vigor – Tier II	85	21 days 6 reps per test group; 5 plants per rep. Concentrations tested: negative control, 18.8, 37.5, 75, 150, 300 g a.i./ha [Concentrations in lbs a.i./Acre: 0.0168, 0.0334, 0.0669, 0.1338, 0.2676 lbs a.i./A]	<u>Most sensitive dicot</u> Pumpkin (*Cucurbita mixta*: Cucurbitaceae)– weight EC_{05}: 0.0071 (0.001-0.05) lbs a.i./A **EC_{25}: 0.0748 (0.03-0.17) lbs a.i./A** EC_{50}: 0.3834 (0.20-0.72) lbs a.i./A **NOAEC: 0.0168 lbs a.i./A** <u>Most sensitive monocot</u> Onion[1] (*Allium cepa*; Liliaceae) – length EC_{05}: 0.2626 (0.25-0.27) lbs a.i./A **EC_{25} >0.2676 lbs a.i./A** EC_{50} >0.2676 lbs a.i./A **NOAEC: 0.2676 lbs a.i./A** Endpoints affected: length (or height), dry weight *Sublethal effects:* Signs of toxicity primarily observed on plants included necrosis, leaf curl, mortality, stem curl, and chlorosis. Generally, monocots did not exhibit treatment-related signs of toxicity, whereas dicots did.	47701639	Supplemental

[1] The ECx's for onion did not indicate convergence whereby an algorithm was not plotted against the data indicating clear inhibition with increasing concentration. As most monocot data had similar results, the onion was chosen on the basis of the lowest EC_{25} of the monocots for which the endpoint was available.

[2] **Bold** values used to calculate risk quotients and/or in risk description

IV. Risk Characterization

A. Risk Estimation –Integration of Exposure and Effects Data

A quantitative estimation of risk integrates EECs and toxicity estimates and evaluates the likelihood of adverse ecological effects to non-target species. In a deterministic approach, an exposure estimate is divided by a single point estimate of toxicity to calculate a risk quotient (RQ). The RQ is then compared to Agency Levels of Concern (LOCs, **Appendix F**), which serve as criteria for categorizing potential risk to non-target organisms and the need to consider regulatory action.

1. Risk to Aquatic Animals and Plants

A majority of the aquatic studies yielded non-definitive endpoints with little to no sublethal effects. For those studies that yielded non-definitive endpoints but presented sublethal effects, endpoints were used in risk description, however, RQs were not calculated; this includes chronic data for freshwater invertebrates and vascular plant data on the degradates (M-1, M-3). Risk quotient calculations were made using definitive endpoints for the vascular (parent only) and non-vascular (parent and degradates: M-1, M-3) aquatic plants, chronic data on the freshwater fish. Chronic data for the marine/estuarine fish and invertebrates were not provided by the registrant; although acute data on these taxa indicate no effect at the highest tested concentrations, risk to these taxa on a chronic basis cannot be precluded. However, equivalent toxicity to freshwater fish and invertebrates is assumed for the estuarine/marine fish and invertebrates, thereby negating the risk conclusion. It is important to note that discussion of corn scenarios in the aquatic assessment below applies to soybeans as well and that non-crop sites include the several scenarios. Therefore, corn/soybean scenarios include IA corn, IL corn, OH corn, and MS corn for pre-emergent, pre-plant, pre-plant (soil incorporated), post-plant, and fall applications; winter wheat scenario includes ND wheat for fall pre-plant applications, and non-crop scenarios include TN nursery, PA apple, and NY grapes.

a. Aquatic Animals

1. *Risk following acute exposure*

<u>Freshwater Fish and Aquatic-Phase Amphibians</u>

The acute aquatic RQs for freshwater fish and aquatic-phase amphibians were not calculated on the basis of a non-definitive endpoint observed in both freshwater fish studies with no sublethal effects. However, taking the lowest limit dose (rainbow trout, MRID 47701626) value and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded.

Freshwater Invertebrates

The acute aquatic RQs for freshwater invertebrates were not calculated on the basis of a non-definitive endpoint with no sublethal effects observed in the provided study. However, taking the limit dose (*Daphnia*, MRID 47701623) value and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded.

Marine/Estuarine Fish

The acute aquatic RQs for marine/estuarine fish were not calculated on the basis of a non-definitive endpoint with no sublethal effects observed in the provided study. However, taking the highest concentration tested (sheepshead minnow, MRID 47701628) and comparing it to the EECs for the corn/soybean scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded.

Marine/Estuarine Invertebrates

The acute aquatic RQs for marine/estuarine invertebrates were not calculated on the basis of a non-definitive endpoint with no sublethal effects observed in the provided study. However, taking the highest concentration tested (saltwater mysid, MRID 47701625) and comparing it to the EECs for the corn/soybean scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded.

2. *Risk following chronic exposure*

Freshwater Fish and Aquatic-Phase Amphibians

The chronic aquatic RQs (all <0.01) for freshwater fish and aquatic-phase amphibians did not exceed the chronic LOC for any of the uses analyzed (the corn, soybean, winter wheat and non-crop uses).

Freshwater Invertebrates

The chronic aquatic RQs for freshwater invertebrates were not calculated on the basis of a non-definitive endpoint observed in the provided study. However, sublethal effects were observed. Taking the highest concentration tested (NOAEC $\geq$ 1.9 mg a.i./L *Daphnia*, MRID 47701629) and comparing it to the EECs for the corn/soybean scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded.

Marine/Estuarine Fish

No chronic studies on marine/estuarine fish were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. Chronic risk to marine/estuarine fish cannot be precluded on this basis alone. However, both freshwater and marine/estuarine acute data indicate that pyroxasulfone is at most, moderately toxic to the tested organisms (*i.e.*, no effects were observed at comparable concentrations) suggesting that a comparison between freshwater and marine/estuarine fish may be appropriate in the particular case of pyroxasulfone. Furthermore, comparison of EEC values with acute endpoints for freshwater and marine/estuarine fish, respectively, as well as chronic RQs (<0.01) for freshwater fish and aquatic-phase amphibians suggest that chronic risk to marine/estuarine fish is not expected.

Marine/Estuarine Invertebrates

No chronic studies on marine/estuarine invertebrates were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. Chronic risk to marine/estuarine invertebrates cannot be precluded on this basis alone. However, both freshwater and marine/estuarine acute data indicate that pyroxasulfone is at most, moderately toxic to the tested organisms (*i.e.*, no effects were observed at the highest concentrations tested) suggesting that a comparison between freshwater and marine/estuarine invertebrates may be appropriate in the particular case of pyroxasulfone. Furthermore, comparison of EEC values with acute endpoints for freshwater and marine/estuarine invertebrates, respectively, as well as chronic RQs (<0.01) for freshwater invertebrates suggest that chronic risk to marine/estuarine invertebrates is not expected.

b. Aquatic Plants

Vascular plants

The RQ calculations (1.03-1.4) based on a duckweed study (EC_{50}: 0.006 mg a.i./L based on frond count, MRID 47701640) using technical grade active ingredient indicate aquatic non-listed plant LOC exceedances for a majority of the corn/soybean scenarios (IL/OH: pre and post plant, MS: pre and post plant, fall application), ND wheat (fall) but not the IA corn scenario, ND wheat (pre-plant) scenario, and non-crop uses. Similarly, the RQ calculations (8.38-46.6) based on the same study (NOAEC 0.00018 mg a.i./L based on frond count) indicate aquatic listed plant LOC exceedances for all of the corn/soybean scenarios (IA/IL/OH/MS), all wheat scenarios (ND pre-plant and ND fall), as well as all non-crop scenarios (TN nursery, PA apple, and NY grapes).

The vascular plant RQs for metabolites (M-1, M-3) were not calculated on the basis of a non-definitive endpoint observed in the provided studies (frond count, biomass, and growth rate, MRIDs 47701641, 47701642). However, sublethal effects were observed. Taking the highest concentration tested (123 mg a.i./L) and comparing it to the EECs for the corn/soybean scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the non-listed and listed plant LOC is not exceeded.

Non-vascular plants

The RQ calculations (3.97- 22.07) based on a freshwater green algae study (EC_{50}: 0.00038 mg a.i./L based on cell density, MRID 47701643) using technical grade active ingredient indicate aquatic non-listed plant LOC exceedances for all corn/soybean scenarios (IA/IL/OH/MS: pre-emergence, pre-plant, pre-plant soil incorporated, post-plant, and fall applications), ND wheat scenarios, and non-crop uses. Similarly, the RQ calculations (15.08 – 83.88) based on the same study (NOAEC 0.0001 mg a.i./L based on cell density) indicates aquatic listed plant LOC exceedances for all corn/soybean scenarios (IA/IL/OH/MS: pre-emergence, pre-plant, pre-plant soil incorporated, post-plant, and fall applications), ND wheat scenarios, and non-crop uses.

The RQ calculations (all <0.01) based on a freshwater green algae study (EC_{50}: 56 mg a.i./L and NOAEC: 31 mg a.i./L based on cell density, MRID 47701647) using metabolite (M-1) indicate no aquatic listed or non-listed plant LOC exceedances for any scenario assessed. Similarly, there are no listed or non-listed plant LOC exceedances for the other metabolite (M-3) tested on the freshwater green algae (EC_{50}: 38 mg a.i./L and NOAEC: 15 mg a.i./L based on cell density, MRID 47701648).

2. Risk to Terrestrial Animals and Plants

a. Terrestrial Animals

To assess risks of pyroxasulfone to non-target birds and mammals, EECs and acute and chronic RQs for residues on various forage categories (short grass, tall grass, broadleaf plants/small insects, fruits/pods/large insects, and seeds) were obtained from the Tier I model, T-REX v. 1.4.1 for broadcast, ground, and/or aerial spray as well as band or soil incorporated applications to the proposed crops. The model assumes initial concentrations on plant surfaces based on Kenaga-predicted maximum residues as modified by Fletcher *et al.* (1994), and assumes first-order dissipation. In this case, one application of 0.267 a.i./A was used to address corn, soybean, winter wheat (per the KIH-485 W85 and Pyroxasulfone 85W labels), 0.096 lbs a.i./A for soy and 0.206 lbs a.i./A for non-crop uses (per the V-10233 Herbicide Water Dispersible Granules Commercial label) and 0.120 lbs a.i./A for corn, soybean, and non-crop uses (per the V-10233 Herbicide label). In all cases, the default foliar dissipation half-life of 35 days was used.

For birds, acute RQs are derived using dose-based and dietary-based acute toxicity values. For mammals, acute RQs are derived using a dose-based acute toxicity value, and chronic RQs are derived using a dose-based chronic toxicity value and a dietary-based chronic toxicity value using the standard FDA laboratory rat conversion value provided in the T-REX model. Dietary-based RQs are calculated using EECs expressed in terms of residue concentration for the various forage categories and toxicity values (LC_{50} or NOAEC) expressed in units of dietary concentration. Dose-based RQs are calculated using a body weight-adjusted LD_{50} and consumption-weighted equivalent dose sorted by food source and body size. For both birds and mammals, three weight categories (or sizes) are considered.

1. ***Risk following acute exposure***

Birds

The acute oral and dietary endpoints are both greater than the highest concentrations tested (LD_{50} >2250 mg a.i./kg bw and LC_{50} >5620 mg a.i./kg diet, respectively). There were no mortalities or treatment related clinical signs of toxicity in the two acute oral studies (bobwhite quail, MRID 47701631; zebra finch, MRID 47701632) and one of the two dietary studies (bobwhite quail, MRID 47701633). However, the dietary study on mallard duck (MRID 47701634) indicated sublethal effects statistically significant from the controls that led to a definitive NOAEC calculation. Nevertheless, the acute RQ values are not reported on account of the non-definitive LD_{50}/LC_{50} values. However, taking the highest concentrations tested and comparing them to the T-REX generated EECs indicates that the lowest LOC (0.1, for listed species) is not exceeded for any of the application rates examined relating to corn, soybean, wheat, and non-crop uses.

Potential risk to piscivorous birds

The potential risk to piscivorous birds considers exposure via consumption of fish contaminated with pyroxasulfone residues. However, given that the log K_{ow} for pyroxasulfone is below the 4-8 range required to trigger use of the KABAM v.1.0, acute RQ values are not reported for this exposure route. Furthermore, substantial bioaccumulation in aquatic food webs is not expected given the low log K_{ow} of pyroxasulfone (2.39).

Mammals

The acute endpoint for mammals is greater than the limit dose (LD_{50} >2000 mg a.i./kg bw, rat, MRID 47701677) for the parent compound. There were no mortalities or treatment related clinical signs of toxicity in the acute oral rat study using the parent compound. Therefore, acute RQ values are not reported. However, taking the tested limit dose and comparing it to the T-REX generated EECs indicates that the lowest LOC (0.1, for listed species) is not exceeded for any of the application rates examined relating to corn, soybean, wheat, and non-crop uses. The seven degradate/metabolite acute oral rat studies had determined the same endpoint value, however, a majority of these studies also indicated sublethal effects in the test animals. Furthermore, two additional studies on two pyroxasulfone formulations determined comparable endpoint values. However, all studies were performed on a small subset of organisms (either one or two groups of three to five female rats), at a limit dose, and without control groups.

Potential risk to piscivorous mammals

The potential risk to piscivorous mammals considers exposure via consumption of fish contaminated with pyroxasulfone residues. However, given that the log K_{ow} for pyroxasulfone is below the 4-8 range required to trigger use of the KABAM v.1.0, acute RQ values are not reported for this exposure route. Furthermore, substantial bioaccumulation in aquatic food webs is not expected given the low log K_{ow} of pyroxasulfone (2.39).

Terrestrial invertebrates

Honeybee

Pyroxasulfone is classified as 'practically non-toxic' to honey bees on an acute contact basis (LD_{50} >100 µg a.i./bee, MRID 47701637) for the technical grade active ingredient. In addition, the interim listed species LOC for terrestrial invertebrates is 0.05. To lead to LOC exceedances (given the toxicity value is 781.25 µg a.i./g of bee, whereby the LD_{50} is 100 µg a.i./bee and one bee weighs approximately 0.128g), the EEC would have to equal or exceed 39 µg a.i./g of bee (or ppm). However, the dietary-based EECs for small (36.05 ppm) and large (4.01 ppm) insects is below this value given the highest *seasonal* maximum application rate of 0.267 lbs a.i./A. Meaning, that the interim LOC is not exceeded at the highest application rates indicated on the labels.

Parasitoid wasp, predatory mite, and earthworm (Non-guideline studies)

The two formulation (WG 85, 84.7% a.i.) studies (wasp, 48-hours long, MRID 47889323; mite, 7-days long, MRID 47701753) indicate that this particular pyroxasulfone formulation is considered to lead to effects (fecundity in both studies and mortality in the mite study) but not in 50% of the population or greater up to the highest concentration tested. Both studies indicate that the ER_{50} and LR_{50} values are greater than the highest concentration tested (*i.e.,* >1000 g a.i./ha).

Given a non-guideline acute earthworm study (14-days long, MRID 47701748) using the technical active ingredient, pyroxasulfone is considered to be non-lethal to earthworms up to a concentration of 997 mg a.i./kg dry soil. Similarly, a non-guideline study (28-days long, MRID Pending) testing earthworm growth and reproduction indicates that mortality and reproductive performance are not affected at soil concentrations up to 1000 ppm (*i.e.*, presumed units of mg a.i./kg dry soil). However, given the persistence of pyroxasulfone in soil (*i.e.*, anaerobic soil metabolism half life is up to 156 days; aerobic soil metabolism half-life is up to 533 days), which is greater than the durations of the submitted studies, the chronic effect to earthworms and other soil dwelling organisms is uncertain at this time.

2. *Risk following chronic exposure*

Birds

Utilizing the chronic endpoint (60 mg a.i./kg diet) from a 1-generation reproduction study (MRID 47701636) conducted with the mallard duck and the T-REX model v.1.4.1, the chronic avian dietary-based RQ exceeds the chronic LOC for birds only for the short grass food item and only for the highest maximum *seasonal* application rate (0.267 lbs a.i./A, see **Table 34**). Assuming that a concentration of 0.0534 lbs a.i./A is applied three days after the maximum single application rate (0.2136 lbs a.i./A) also leads to a chronic LOC exceedance (*i.e.*, RQ is 1.02) for birds for the short grass food item (Table 34).

Table 34. Upper Bound Kenaga, Chronic Avian Dietary Based Risk Quotients

NOAEC (ppm)	EECs and RQs[1,2,3]							
	Short Grass		Tall Grass		Broadleaf Plants/ Small Insects		Fruits/Pods/ Seeds/ Large Insects	
	EEC	RQ	EEC	RQ	EEC	RQ	EEC	RQ
60[a]	64.08	**1.07**[4]	29.37	0.49	36.05	0.60	4.01	0.07
60[b]	49.44	0.82	22.66	0.38	27.81	0.46	3.09	0.05
60[c]	28.80	0.48	13.20	0.22	16.20	0.27	1.80	0.03
60[d]	23.04	0.38	10.56	0.18	12.96	0.22	1.44	0.02
60[e]	61.20	**1.02**[4]	28.05	0.47	34.43	0.57	3.83	0.06

[1] Risk Quotients are calculated using the following formula: EEC / NOAEC
[2] Chronic risk LOC = 1
[3] Based on avian chronic NOAEC = 60 mg a.i./kg diet
[4] **Bolded** values exceed LOC
[a] Single application at the maximum seasonal rate of 0.267 lbs a.i./A for corn, soybean, and winter wheat (KIH-485 W85 and Pyroxasulfone 85W labels)
[b] Single application at the maximum seasonal rate of 0.206 lbs a.i./A for non-crop sites (V-10233 Herbicide Water Dispersible Granules commercial label)
[c] Single application at the maximum seasonal rate of 0.120 lbs a.i./A for corn, soybean, fallow land, and non-crop sites (V-10233 Herbicide label)
[d] Single application at the maximum seasonal rate of 0.096 lbs a.i./A for soybean (V-10233 Herbicide Water Dispersible Granules commercial label)
[e] Two applications of variable value applied at a 3-day interval. The application of 0.2136 lbs a.i./A (the maximum single application rate) and 0.0534 lbs a.i./A sum to the maximum seasonal application rate of 0.267 lbs a.i./A.

Potential risk to piscivorous birds

The potential risk to piscivorous birds considers exposure via consumption of fish contaminated with pyroxasulfone residues. However, given that the log K_{ow} for pyroxasulfone is below the 4-8 range required to trigger use of the KABAM v.1.0, chronic RQ values are not reported for this exposure route. Furthermore, substantial bioaccumulation in aquatic food webs is not expected given the low log K_{ow} of pyroxasulfone (2.39).

<u>Mammals</u>

Utilizing the chronic endpoint (7.2 mg a.i./kg-bw parental toxicity for male rats; equivalent to 100 mg a.i./kg-diet) from a 2-generation reproduction study (MRID 47701706) conducted with the rat and the T-REX model v.1.4.1, the chronic mammalian *dietary-based* RQs do not exceed the chronic LOC for mammals. However, the chronic mammalian *dose-based* RQs do exceed the chronic LOC for mammals for the short grass food item (in all size classes: 15, 35, and 1000g) as well as the tall grass and broadleaf plants/small insects categories (in the smaller two size classes: 15 and 35 g) for a couple of maximum seasonal application rates (0.267 lbs a.i./A, 0.206 lbs a.i./A see **Table 35**). LOC exceedances for the short grass food item (in the smaller two size classes: 15 and 35g) occurs for the remaining maximum seasonal application rates (0.120 lbs a.i./A and 0.096 lbs a.i./A, Table 35).

Table 35. Upper Bound Kenaga, Chronic Mammalian Dose-Based Risk Quotients

Size Class (grams)	Adjusted NOAEL	EECs and RQs[1,2,3]									
		Short Grass		Tall Grass		Broadleaf Plants/ Small Insects		Fruits/Pods/ Seeds/ Large Insects		Granivore	
		EEC	RQ	EEC	RQ	EEC	RQ	EEC	RQ	EEC	RQ
15[a]	15.82	61.10	**3.86**[4]	28.00	**1.77**	34.37	**2.17**	3.82	0.24	0.85	0.05
35[a]	12.80	42.23	**3.30**	19.35	**1.51**	23.75	**1.86**	2.64	0.21	0.59	0.05
1000[a]	5.54	9.79	**1.77**	4.49	0.81	5.51	0.99	0.61	0.11	0.14	0.02
15[b]	15.82	47.14	**2.98**	21.60	**1.37**	26.51	**1.68**	2.95	0.19	0.65	0.04
35[b]	12.80	32.58	**2.54**	14.93	**1.17**	18.33	**1.43**	2.04	0.16	0.45	0.04
1000[b]	5.54	7.55	**1.36**	3.46	0.63	4.25	0.77	0.47	0.09	0.10	0.02
15[c]	15.82	27.46	**1.74**	12.59	0.80	15.45	0.98	1.72	0.11	0.38	0.02
35[c]	12.80	18.98	**1.48**	8.70	0.68	10.67	0.83	1.19	0.09	0.26	0.02
1000[c]	5.54	4.40	0.79	2.02	0.36	2.48	0.45	0.28	0.05	0.06	0.01
15[d]	15.82	21.97	**1.39**	10.07	0.64	12.36	0.78	1.37	0.09	0.31	0.02
35[d]	12.80	15.18	**1.19**	6.96	0.54	8.54	0.67	0.95	0.07	0.21	0.02
1000[d]	5.54	3.52	0.64	1.61	0.29	1.98	0.36	0.22	0.04	0.05	0.01

[1] Risk Quotients are calculated using the following formula: EEC / NOAEC
[2] Chronic risk LOC = 1
[3] Based on mammalian chronic dose-based NOAEL: 7.2 mg a.i./kg bw/day
[4] **Bolded** values exceed LOC
[a] Single application at the maximum seasonal rate of 0.267 lbs a.i./A for corn, soybean, and winter wheat (KIH-485 W85 and Pyroxasulfone 85W labels)
[b] Single application at the maximum seasonal rate of 0.206 lbs a.i./A for non-crop sites (V-10233 Herbicide Water Dispersible Granules commercial label)
[c] Single application at the maximum seasonal rate of 0.120 lbs a.i./A for corn, soybean, fallow land, and non-crop sites (V-10233 Herbicide label)
[d] Single application at the maximum seasonal rate of 0.096 lbs a.i./A for soybean (V-10233 Herbicide Water Dispersible Granules commercial label)

Potential risk to piscivorous mammals

The potential risk to piscivorous mammals considers exposure via consumption of fish contaminated with pyroxasulfone residues. However, given that the log K_{ow} for pyroxasulfone is below the 4-8 range required to trigger use of the KABAM v.1.0, chronic RQ values are not reported for this exposure route. Furthermore, substantial bioaccumulation in aquatic food webs is not expected given the low log K_{ow} of pyroxasulfone (2.39).

b. Terrestrial Plants

Utilizing the toxicity endpoints (MRID 47701638 - seedling emergence: monocot EC_{25} = 0.0669 lbs a.i./A, NOAEC = 0.0168 lbs a.i./A and dicot EC_{25} = 0.2615 lbs a.i./A, NOAEC = 0.1338 lbs a.i./A; MRID 47701639 - vegetative vigor: monocot EC_{25} > 0.2676 lbs a.i./A, NOAEC = 0.2676 lbs a.i./A and dicot EC_{25} = 0.0748 lbs a.i./A, NOAEC = 0.0168 lbs a.i./A), assuming liquid ground spray (1% drift fraction) and aerial spray (5% drift fraction) application method, a default incorporation depth of 1 inch, and a solubility limit in water of 3.49 mg/L (at 25°C), the RQ calculations indicate that monocots in semi-aquatic areas exposed to runoff and spray drift from either ground or aerial spray applications are most sensitive given that the listed species LOC (of 1) is exceeded for several maximum *seasonal* application rates (0.267 lbs a.i./A, 0.206 lbs a.i./A for ground spray applications and 0.120 lbs a.i./A for aerial spray applications, see **Table 36**). Changing the application rate from 0.267 to 0.2136 lbs a.i./A (the maximum single application rate) alters the RQ from 1.75 to 1.40 but does not change the risk conclusion for ground spray applications with KIH-485/Pyroxasulfone W85 formulations. The maximum *seasonal* and maximum single application rate for the V-10233 Herbicide Water Dispersible Granules commercial label is the same (*i.e.*, 0.206 lbs a.i./A); therefore, the RQ calculations and risk conclusions for ground spray applications with this formulation do not change. Similarly, the maximum *seasonal* and maximum single application rate for the V-10233 Herbicide label, which is the only label with proposed aerial spray applications, is the same (*i.e.*, 0.120 lbs a.i./A); therefore, the RQ calculations and risk conclusions specifically regarding aerial spray applications with this formulation do not change.

Table 36. RQ values for plants in dry and semi-aquatic areas exposed to Pyroxasulfone through runoff and/or spray drift[1,2]				
Plant Type	**Listed Status**	**Dry**	**Semi-Aquatic**	**Spray Drift**
Ground spray (1% drift fraction)				
Monocot[a]	non-listed	<0.1	0.44	<0.1
Monocot[a]	listed	0.32	**1.75**[3]	0.16
Dicot[a]	non-listed	<0.1	0.11	<0.1
Dicot[a]	listed	<0.1	0.22	0.16
Monocot[b]	non-listed	<0.1	0.34	<0.1
Monocot[b]	listed	0.25	**1.35**[3]	0.12
Dicot[b]	non-listed	<0.1	<0.1	<0.1
Dicot[b]	listed	<0.1	0.17	0.12
Monocot[c]	non-listed	<0.1	0.20	<0.1
Monocot[c]	listed	0.14	0.79	<0.1
Dicot[c]	non-listed	<0.1	<0.1	<0.1
Dicot[c]	listed	<0.1	<0.1	<0.1
Monocot[d]	non-listed	<0.1	0.16	<0.1
Monocot[d]	listed	0.11	0.63	<0.1
Dicot[d]	non-listed	<0.1	<0.1	<0.1
Dicot[d]	listed	<0.1	<0.1	<0.1
Aerial Spray (5% drift fraction)				
Monocot[c]	non-listed	0.11	0.27	<0.1
Monocot[c]	listed	0.43	**1.07**[3]	0.36
Dicot[c]	non-listed	<0.1	<0.1	<0.1
Dicot[c]	listed	<0.1	0.13	0.36

[1] Risk Quotients are calculated using the following formula: EEC / NOAEC or EC_{05} (listed); EEC / EC_{25} (non-listed)
[2] Chronic risk LOC = 1. If RQ > 1.0, the LOC is exceeded, resulting in potential for risk to that plant group.
[3] **Bolded** values exceed LOC
[a] Single application at the maximum seasonal rate of 0.267 lbs a.i./A for corn, soybean, and winter wheat (KIH-485 W85 and Pyroxasulfone 85W labels)
[b] Single application at the maximum seasonal rate of 0.206 lbs a.i./A for non-crop sites (V-10233 Herbicide Water Dispersible Granules commercial label)
[c] Single application at the maximum seasonal rate of 0.120 lbs a.i./A for corn, soybean, fallow land, and non-crop sites (V-10233 Herbicide label)
[d] Single application at the maximum seasonal rate of 0.096 lbs a.i./A for soybean (V-10233 Herbicide Water Dispersible Granules commercial label)

Contamination via irrigation water

Predicted groundwater concentrations of pyroxasulfone (equivalent to the equilibrium concentration taken over a 30 year period) were used to estimate the potential phytotoxic effects from irrigation water to plants and sensitive crops on the treated field**.** It is assumed that a one-acre field is irrigated with one inch of water containing pyroxasulfone at the equilibrium concentration. **Table 37** illustrates the RQ calculations obtained given the estimated concentrations. There are no non-listed plant LOC exceedances (on the basis of EEC/ EC_{25}); however, given the estimates for the DE and WI scenarios, listed plant LOCs are exceeded (on the basis of EEC/NOAEC) with RQs of 1.12 and 2.01 for both monocot and dicot species, which implies that effects may be expected for listed species that may be on the irrigated field.

Table 37. Estimated Concentrations in Soil from Irrigation Water and RQs for Terrestrial Plants					
Scenario	**Post Breakthrough Average (ppb)**	**EECs (lbs a.i./A)[1]**	**Monocot non-listed RQ[2]**	**Dicot non-listed RQ[2]**	**Monocot & Dicot listed RQ[4]**
GA Peanuts	28.7	0.007	0.10	0.09	0.39
FL Potato	38.2	0.009	0.13	0.12	0.52
FL Citrus	54.7	0.012	0.19	0.17	0.74
DE Sweet Corn	83	0.019	0.28	0.25	**1.12**[5]
NC Cotton	43.4	0.010	0.15	0.13	0.59
WI Corn	149	0.034	0.50	0.45	**2.01**[5]
SCIGROW	1.93	0	0.01	0.01	0.03

[1] EEC calculation: Assuming a one-acre field is irrigated with one inch of water containing pyroxasulfone. One acre has 6,272,640 cubic inches of water on the field. The1 acre field with 1 inch of water has 3,630 cubic ft of water (6,272,640 x 0.00058 cubic ft/cubic inch). The field has 27,156 gallons of water (3,630 cubic ft x 7.481 gallons/cubic ft). Therefore, 1 inch of water on the 1 acre field weighs 226,625 lbs (27,156 gallons x 8.3453 lbs/gallon of water).

$$\frac{\text{226,625 lb of water/acre * [post breakthrough ave in ppb]}}{\text{1,000,000,000}} = \text{EEC in lbs a.i./A}$$

[2] Based on seedling emergence study (MRID 47701638) most sensitive monocot, onion EC_{25} = 0.0669 lbs a.i./A
[3] Based on vegetative vigor study (MRID 47701639) most sensitive dicot, pumpkin EC_{25} = 0.0748 lbs a.i./A
[4] Based on the studies and species from footnotes 2 and 3 above; NOAEC = 0.0168 lbs a.i./A for both species
[5] **Bold** values indicate listed plant LOC exceedance given EEC/ NOAEC > 1

B. Risk Description

Based on the available ecotoxicity data and predicted environmental exposures, risks to aquatic (non-vascular and vascular, listed and non-listed) and terrestrial (listed) plants as well as non-listed and listed birds and mammals following chronic exposure are expected. The pyroxasulfone degradates, M-1 and M-3, are not considered degradates of concern for duckweed (vascular aquatic plant) or freshwater green algae (non-vascular aquatic plant). The pyroxasulfone degradates, M-1, M-3, M-25, I-3, I-4, I-5, M-28, are not considered degradates of concern for mammals (on an acute basis). The formulations WG85 (84.7% a.i.) and V-10233 (42.2% pyroxasulfone; 33.6% flumioxazin) are not considered to pose a risk to mammals (on an acute basis). The formulation WG85 (84.7% a.i.) is considered to not pose a risk to (non-guideline) terrestrial invertebrates (parasitoid wasp, predatory mite).

1. Risk to Aquatic Animals and Plants

a. Aquatic Animals

1. *Risk following acute exposure*

Freshwater Fish and Aquatic-Phase Amphibians

Technical

The acute aquatic RQs for freshwater fish and aquatic-phase amphibians were not calculated on the basis of a non-definitive endpoint observed in both freshwater fish studies with no sublethal effects. However, taking the lowest limit dose (2.2 mg a.i./L for rainbow trout, MRID 47701626) value and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. Given these studies and assuming that pyroxasulfone concentrations in the environment reach the solubility limit, the effect of the technical grade active ingredient on freshwater fish is likely to be low. However, according to the model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), levels of pyroxasulfone at the solubility limit are not expected to occur in surface water given the proposed corn, soybean, wheat, and non-crop uses. Therefore, acute risk to freshwater fish and aquatic-phase amphibians is not expected as a result of pyroxasulfone use on corn, wheat, and non-crop sites given the results from the studies using technical grade active ingredient.

Metabolites/Degradates

No acute data on metabolites/degradates for freshwater fish and aquatic-phase amphibians was provided. Risk cannot be precluded on the basis of no data available.

Formulations

No acute data on formulations of pyroxasulfone for freshwater fish and aquatic-phase amphibians was provided. Risk cannot be precluded on the basis of no data available.

Freshwater Invertebrates

Technical

The acute aquatic RQs for freshwater invertebrates were not calculated on the basis of a non-definitive endpoint with no sublethal effects observed in the provided study. However, taking the limit dose (4.4 mg a.i./L, *Daphnia*, MRID 47701623) value and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. However, for the particular study and on account of poor solubility, column elution methodology was utilized to achieve saturation at the limit dose, a higher value. The difference in reported solubility limits may be a factor of water quality parameters such as pH and dissolved salts. Given this study and assuming that pyroxasulfone concentrations in the environment reach the solubility limit, the effect of the technical grade active ingredient on freshwater invertebrates is likely to be low. According to the model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), levels of pyroxasulfone at the solubility limit are not expected to occur in surface water given the proposed corn, wheat, and non-crop uses. Therefore, acute risk to freshwater invertebrates is not expected as a result of pyroxasulfone use on corn, soybean, wheat, and non-crop sites given the results from the Daphnid study using technical grade active ingredient.

Metabolites/Degradates
No acute data on metabolites/degradates for freshwater invertebrates was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute data on formulations of pyroxasulfone for freshwater invertebrates was provided. Risk cannot be precluded on the basis of no data available.

Marine/Estuarine Fish

The acute aquatic RQs for marine/estuarine fish were not calculated on the basis of a non-definitive endpoint with no sublethal effects observed in the provided study. However, taking the highest concentration tested (3.3 mg a.i./L sheepshead minnow, MRID 47701628) and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. Given this study and assuming that pyroxasulfone concentrations in the environment reach the solubility limit, the effect of the technical grade active ingredient on marine/estuarine fish is likely to be low. According to the model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), levels of pyroxasulfone at the solubility limit or at the highest concentration tested are not expected to occur in surface water given the proposed corn, wheat, and non-crop uses. Therefore, acute risk to marine/estuarine fish is not expected as a result of pyroxasulfone use on corn, soybean, wheat, and non-crop sites given the results from the sheepshead minnow study using technical grade active ingredient.

Metabolites/Degradates
No acute data on metabolites/degradates for marine/estuarine fish was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute data on formulations of pyroxasulfone for marine/estuarine fish was provided. Risk cannot be precluded on the basis of no data available.

Marine/Estuarine Invertebrates

The acute aquatic RQs for marine/estuarine invertebrates were not calculated on the basis of a non-definitive endpoints with no sublethal effects observed in the provided studies (although one mortality was observed at the lowest test concentration but was not considered treatment related in the saltwater mysid study). However, taking the highest concentration tested (1.4 mg a.i./L, saltwater mysid, MRID 47701625) and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. Given this study and assuming that pyroxasulfone concentrations in the environment reach the solubility limit, the effect of the technical grade active ingredient on marine/estuarine invertebrates is likely to be low. According to the model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), levels of pyroxasulfone at the solubility limit or at the highest concentration tested are not expected to occur in surface water given the proposed corn, wheat, and non-crop uses. Therefore, acute risk to marine/estuarine invertebrates is not expected as a result of pyroxasulfone use on corn, soybean, wheat, and non-crop sites given the results from the saltwater mysid study using technical grade active ingredient.

Metabolites/Degradates
No acute data on metabolites/degradates for marine/estuarine invertebrates was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute data on formulations of pyroxasulfone for marine/estuarine invertebrates was provided. Risk cannot be precluded on the basis of no data available.

2. ***Risk following chronic exposure***

Freshwater Fish and Aquatic-Phase Amphibians

The chronic aquatic RQs for freshwater fish and aquatic-phase amphibians did not exceed the chronic LOC for any of the uses analyzed (the corn, wheat and non-crop uses). The RQ was based on the 28-day NOAEC of 2.0 mg a.i./L from the chronic fathead minnow study (MRID 47701630). In this study, there was a significant reduction in percent survival relative to the controls in the second lowest mean-measured concentration tested (0.58 mg a.i./L) but was not considered treatment related. Sublethal effects were observed in the study such as weakness, small size, and a curled/crooked spine, but the frequency of these effects did not appear to differ from the controls. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. Given this study (the 28-day LOAEC is 3.9 mg a.i./L) and assuming that pyroxasulfone concentrations in the environment reach the solubility limit and persist for at least 109 days (per aerobic aquatic metabolism half-life study; note that the duration of the chronic fish study is 28-days), the effect of the technical grade active ingredient on freshwater fish and aquatic-phase amphibians is still likely to be low. According to the model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), levels of pyroxasulfone at the solubility limit or at the highest concentration tested are not expected to occur in surface water given the proposed corn, soybean, wheat, and non-crop uses. Therefore, chronic risk to freshwater fish and aquatic-phase amphibians is not expected as a result of pyroxasulfone use on corn, wheat, and non-crop sites given the results from the fathead minnow study using technical grade active ingredient.

Metabolites/Degradates
No chronic data on metabolites/degradates for freshwater fish and aquatic-phase amphibians was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute data on formulations of pyroxasulfone for freshwater fish and aquatic-phase amphibians was provided. Risk cannot be precluded on the basis of no data available.

Freshwater Invertebrates

The chronic aquatic RQs for freshwater invertebrates were not calculated on the basis of a non-definitive endpoint observed in the provided study. However, sublethal effects were observed such as pale discoloration, injury, and lethargy, which were infrequent, comparable to controls, and not considered treatment related. Taking the highest concentration tested (1.9 mg a.i./L, *Daphnia*, MRID 47701629) and comparing it to the EECs for the corn scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the lowest LOC (0.05, for listed species) is not exceeded. The pyroxasulfone limit of water solubility is reported as 3.49 mg/L at 25°C. Given this study (the 21-day LOAEC is >1.9 mg a.i./L) and assuming that pyroxasulfone concentrations in the environment reach the solubility limit and persist for at least 109 days (per aerobic aquatic metabolism half-life study; note that the duration of the chronic fish study is 28-days), the effect of the technical grade active ingredient on freshwater invertebrates is unknown since the study did not test up to the solubility limit. However, the effect is likely to be low given that model estimated EECs (0.002 - 0.008 mg/L, which includes pyroxasulfone only residues), suggest that levels of pyroxasulfone at the solubility limit or at the highest concentration tested are not expected to occur in surface water given the proposed corn, wheat, and non-crop uses. Therefore, chronic risk to freshwater invertebrates is not expected as a result of pyroxasulfone use on corn, soybean, wheat, and non-crop sites given the results from the *Daphnia* study using technical grade active ingredient.

Metabolites/Degradates
No chronic data on metabolites/degradates for freshwater invertebrates was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute data on formulations of pyroxasulfone for freshwater invertebrates was provided. Risk cannot be precluded on the basis of no data available.

Marine/Estuarine Fish

No chronic studies on marine/estuarine fish were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. Chronic risk to marine/estuarine fish cannot be precluded on the basis of no data available for the technical grade active ingredient, metabolite/degradate, or formulation. However, both freshwater and marine/estuarine acute data indicate that pyroxasulfone is at most, moderately toxic to the tested organisms (*i.e.*, no effects were observed at comparable concentrations) suggesting that a comparison between freshwater and marine/estuarine fish may be appropriate in the particular case of pyroxasulfone. Therefore, given the results of the freshwater fish analysis (fathead minnow study using technical grade active ingredient), and assuming that marine/estuarine organisms are of approximately equal sensitivity to pyroxasulfone as freshwater organisms are, chronic risk to marine/estuarine fish is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean, wheat, and non-crop sites.

Marine/Estuarine Invertebrates

No chronic studies on marine/estuarine invertebrates were submitted by the registrant. Therefore, a quantitative estimation of risk cannot be conducted. Chronic risk to marine/estuarine invertebrates cannot be precluded on the basis of no data available for the technical grade active ingredient, metabolite/degradate, or formulation. However, both freshwater and marine/estuarine acute data indicate that pyroxasulfone is at most, moderately toxic to the tested organisms (*i.e.*, no effects were observed at the highest concentrations tested) suggesting that a comparison between freshwater and marine/estuarine invertebrates may be appropriate in the particular case of pyroxasulfone. Therefore, given the results of the freshwater invertebrate analysis (*Daphnia* study using technical grade active ingredient), and assuming that marine/estuarine organisms are of approximately equal sensitivity to pyroxasulfone as freshwater organisms are, chronic risk to marine/estuarine invertebrates is not expected as a result of pyroxasulfone (TGAI) use on corn, soybean, wheat, and non-crop sites.

b. Aquatic Plants

Vascular plants

Technical

The RQ calculations (1.03-1.4) based on a duckweed study (EC_{50}: 0.006 mg a.i./L based on frond count, MRID 47701640) using technical grade active ingredient indicate aquatic non-listed plant LOC exceedances for a majority of the corn/soybean scenarios (IL/OH: pre and post plant, MS: pre and post plant, fall application), ND wheat (fall) but not the IA corn scenario, ND wheat (pre-plant) scenario, and non-crop uses. Similarly, the RQ calculations (8.38-46.6) based on the same study (NOAEC 0.00018 mg a.i./L based on frond count) indicate aquatic listed plant LOC exceedances for all of the corn/soybean scenarios (IA/IL/OH/MS), all wheat scenarios (ND pre-plant and ND fall), as well as all non-crop scenarios (TN nursery, PA apple, and NY grapes). Biomass and growth rate were also affected in the study and sublethal effects were noted including root destruction, curled fronds, small fronds, chlorotic and necrotic plants. Given the sensitivity of aquatic vascular plants to pyroxasulfone and expected surface water concentrations, risk to aquatic listed and non-listed vascular plants is expected as a result of pyroxasulfone use on corn, soybeans, wheat, and non-crop uses (listed species).

Metabolites/Degradates
The vascular plant RQs for metabolites (M-1, M-3) were not calculated on the basis of a non-definitive endpoint observed in the provided studies (frond count, biomass, and growth rate, MRIDs 47701641, 47701642). However, sublethal effects (chlorosis and necrosis) were observed in both studies. Taking the highest concentration tested (123 mg a.i./L) and comparing it to the EECs for the corn/soybean scenarios (IA, IL, OH, MS), wheat and non-crop uses indicates that the plant LOC is not exceeded. There is some uncertainty in these estimates as the EECs are based on pyroxasulfone residues only and the solubility limit of these metabolites was not provided by the registrant. However, surface water modeling for total residues (parent+M1+M3) showed small difference in exposure concentrations when compared with modeling for the parent and EPISuite calculations indicate that the solubility limit of these degradates is large (M-1: 15,990 – 984,030 mg/L; M-3: 206.9-458 mg/L) relative to the parent (approximately 3.49 mg/L). Overall, risk to aquatic listed and non-listed vascular plants is not expected as a result of exposure to metabolites of pyroxasulfone post-use on corn, soybean, wheat, and non-crop sites.

Formulations
No aquatic vascular plant data on formulations of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

Non-vascular plants
Technical
The RQ calculations (3.97- 22.07) based on a freshwater green algae study (EC_{50}: 0.00038 mg a.i./L for cell density, MRID 47701643) using technical grade active ingredient indicate non-listed aquatic plant LOC exceedances for all corn/soybean scenarios (IA/IL/OH/MS: pre-emergence, pre-plant, pre-plant soil incorporated, post-plant, and fall applications), ND wheat scenarios, and non-crop uses. Similarly, the RQ calculations (15.08 – 83.88) based on the same study (NOAEC 0.0001 mg a.i./L based on cell density) indicates aquatic listed plant LOC exceedances for all corn/soybean scenarios (IA/IL/OH/MS: pre-emergence, pre-plant, pre-plant soil incorporated, post-plant, and fall applications), ND wheat scenarios, and non-crop uses. Given the sensitivity of aquatic non-vascular plants to pyroxasulfone and expected surface water concentrations, risk to listed and non-listed aquatic non-vascular plants is expected as a result of pyroxasulfone use on corn, soybean, wheat, and non-crop sites.

Metabolites/degradates

The RQ calculations (all <0.01) based on a freshwater green algae study (EC_{50}: 56 mg a.i./L and NOAEC: 31 mg a.i./L based on cell density, MRID 47701647) using metabolite (M-1) indicate no aquatic listed or non-listed plant LOC exceedances for any scenario assessed. Similarly, there are no listed or non-listed plant LOC exceedances for the other metabolite (M-3) tested on the freshwater green algae (EC_{50}: 38 mg a.i./L and NOAEC: 15 mg a.i./L based on cell density, MRID 47701648). There is some uncertainty in these estimates as the EECs are based on pyroxasulfone residues only and the solubility limit of these metabolites was not provided by the registrant. However, surface water modeling for total residues (parent+M1+M3) showed small difference in exposure concentrations when compared with modeling for the parent and EPISuite calculations indicate that the solubility limit of these degradates is large (M-1: 15,990 – 984,030 mg/L; M-3: 206.9-458 mg/L) relative to the parent (approximately 3.49 mg/L). Overall, risk to aquatic non-vascular plants is <u>not</u> expected as a result of exposure to metabolites of pyroxasulfone post-use on corn, soybean, wheat, and non-crop sites.

Formulations

No aquatic non-vascular plant data on formulations of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

2. Risk to Terrestrial Animals and Plants

a. Terrestrial Animals

1. *Risk following acute exposure*

<u>Birds</u>

Technical

The acute oral and dietary endpoints are both greater than the highest concentrations tested (LD_{50} >2250 mg a.i./kg bw and LC_{50} >5620 mg a.i./kg diet, respectively). There were no mortalities or treatment related clinical signs of toxicity in the two acute oral studies (bobwhite quail, MRID 47701631; zebra finch, MRID 47701632) and one of the two dietary studies (bobwhite quail, MRID 47701633). However, the dietary study on mallard duck (MRID 47701634) indicated sublethal effects statistically significant from the controls that led to a definitive NOAEC calculation. Nevertheless, the acute RQ values are not reported on account of the non-definitive LD_{50}/LC_{50} values. However, taking the highest concentrations tested and comparing them to the T-REX generated EECs indicates that the lowest LOC (0.1, for listed species) is not exceeded for any of the application rates examined relating to corn, soybean, wheat, and non-crop uses. Therefore, risk to birds is <u>not</u> expected as a result of exposure to pyroxasulfone post-use on corn, soybean, wheat, and non-crop sites.

Metabolites/degradates

No acute avian data on metabolites/degradates of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No acute avian data on formulations of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

Mammals
Technical, degradates/metabolites, formulations
The acute endpoint for mammals is greater than the limit dose (LD_{50} >2000 mg a.i./kg bw, rat, MRID 47701677) for the parent compound. There were no mortalities or treatment related clinical signs of toxicity in the acute oral rat study using the parent compound. Therefore, acute RQ values are not reported. However, taking the tested limit dose and comparing it to the T-REX generated EECs indicates that the lowest LOC (0.1, for listed species) is not exceeded for any of the application rates examined relating to corn, soybean, wheat, and non-crop uses. The seven degradate/metabolite (M-1, M-3, M-25, I-3, I-4, I-5, M-28) acute oral rat studies had determined the same endpoint value as the technical grade active ingredient, however, a majority of these studies also indicated sublethal effects in the test animals including, but not limited to, decreased respiratory rate, underactivity, lethargy, and body weight loss, which could affect survival of individual mammals in the short term should exposure to these degradates occur. Furthermore, two additional studies on two pyroxasulfone formulations determined comparable endpoint values. However, all studies were performed on a small subset of organisms (either one or two groups of three to five female rats), at a limit dose, and without control groups. Given the comparison to T-REX generated EECs of the technical (as well as degradates/metabolites) and formulation based endpoints, risk to mammals is not expected as a result of exposure to the parent, degradates/metabolites, and formulations of pyroxasulfone post-use on corn, soybean, wheat, and non-crop sites.

Terrestrial invertebrates
Honeybees
Pyroxasulfone is classified as 'practically non-toxic' to honey bees on an acute contact basis (LD_{50} >100 μg a.i./bee, MRID 47701637) for the technical grade active ingredient. Although sublethal effects were observed (*i.e.*, lethargy, loss of equilibrium, and immobility) these were sporadic and not considered treatment related. In addition, the interim listed species LOC for terrestrial invertebrates is 0.05. To lead to LOC exceedances (given the toxicity value is 781.25 μg a.i./g of bee, whereby the LD_{50} is 100 μg a.i./bee and one bee weighs approximately 0.128g), the EEC would have to equal or exceed 39 μg a.i./g of bee (or ppm). However, the dietary-based EECs for small (36.05 ppm) and large (4.01 ppm) insects is below this value given the highest *seasonal* maximum application rate of 0.267 lbs a.i./A. Meaning, that the interim LOC is not exceeded at the highest application rates indicated on the labels for corn, soybean, winter wheat, fallow land, and non-crop sites. Thus, risk to honeybees is not expected as a result of direct contact with pyroxasulfone. Label language for the honeybee is, therefore, not required.

Parasitoid wasp, predatory mite, and earthworm (Non-guideline studies)
The two formulation (WG 85, 84.7% a.i.) studies (wasp, 48-hours long, MRID 47889323; mite, 7-days long, MRID 47701753) indicate that this particular pyroxasulfone formulation is considered to lead to effects (fecundity in both studies and mortality in the mite study) but not in 50% of the population or greater up to the highest concentration tested. Both studies indicate that the ER_{50} and LR_{50} values are greater than the highest concentration tested (*i.e.,* >1000 g a.i./ha = 0.892 lbs a.i./A). Given that the highest tested concentration is approximately 3x greater than the maximum *seasonal* proposed rate (0.267 lbs a.i./A), risk to wasps and mites is not expected as a result of pyroxasulfone use on corn, soybean, winter wheat, fallow land, and non-crop sites.

Given a non-guideline acute earthworm study (14-days long, MRID 47701748) using the technical active ingredient, pyroxasulfone is considered to be non-lethal to earthworms up to a concentration of 997 mg a.i./kg dry soil. Similarly, a non-guideline study (28-days long, MRID Pending) testing earthworm growth and reproduction indicates that mortality and reproductive performance are not affected at soil concentrations up to 1000 ppm (*i.e.*, presumed units of mg a.i./kg dry soil).

E. fetida is found in topsoil at depths of approximately 5-20cm. Given a soil depth of 20 cm and assuming a *seasonal* maximum application rate (0.267 lbs a.i./A, which assumes a hypothetical maximum active ingredient loading rate since the seasonal rate would not be applied all at once), the EEC is much lower (0.114 mg/kg soil) than the concentrations generated in these studies. At shallower depths (5 cm), the EEC is higher (0.458 mg/kg soil), but still lower than maximum concentrations in the studies (997 and 1000 mg a.i./kg soil). Therefore, risk to earthworms is not expected as a result of pyroxasulfone use on corn, soybean, winter wheat, fallow land, and non-crop sites. However, given the persistence of pyroxasulfone in soil (*i.e.*, anaerobic soil metabolism half life is up to 156 days; aerobic soil metabolism half-life is up to 533 days), which is greater than the durations of the submitted studies, the chronic effect to earthworms and other soil dwelling organisms is uncertain at this time.

2. *Risk following chronic exposure*

Birds

Utilizing the chronic endpoint (60 mg a.i./kg diet) from a 1-generation reproduction study (MRID 47701636) conducted with the mallard duck and the T-REX model v.1.4.1, the chronic avian dietary-based RQ (1.07) exceeds the chronic LOC of 1 for birds only for the short grass food item and only for the highest maximum *seasonal* application rate of 0.267 lbs a.i./A found for all crop uses (corn, soybean, and winter wheat). Assuming that a concentration of 0.0534 lbs a.i./A is applied three days after the maximum single application rate (0.2136 lbs a.i./A) also leads to a chronic LOC exceedance (*i.e.*, RQ is 1.02) for birds for the short grass food item (Table 34). The chronic endpoint is based on biologically significant effects on reproductive performance (*i.e.*, hatchability), not statistically significant results. According to OCSPP guidance 850.2300, normal values for hatchability for mallards are between 50 and 90%; when hatchability above 50% per pair was considered, it was found that in the control group, hatchability was at or above 50% in 11 of the 15 pairs (*i.e.*, those alive and with hatchlings; a total of 16 pairs were used in the study), while in the 240 and 600 mg a.i./kg-diet treatment groups only 2 and 5, respectively, out of 13 pairs were above 50%; the 60 mg a.i./kg-diet was comparable to the control with 10 of 12 pairs above 50%. The means (standard deviation) for hatchability across the control and three test concentrations are 59% (25), 74% (19), 39% (21), and 28% (27), which includes pairs for which eggs were set but not hatched – this makes for 16 pairs in the control, 12, 14, and 14 in the respective concentrations. As a result, there appears to be a dose-dependent effect on hatchability, which leads to a NOAEC of 60 mg a.i./kg-diet and the LOAEC 240 mg a.i./kg-diet. Therefore, given the biologically significant effect on hatchability, the persistence of pyroxasulfone, and that the LOCs were exceeded for the given maximum *seasonal* application and multiple applications at potential single applications, chronic risk to birds <u>is expected</u> as a result of pyroxasulfone use on corn, soybean, and winter wheat. Reducing the maximum seasonal application rate would alleviate the risk concern.

Metabolites/degradates
No chronic avian data on metabolites/degradates of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No chronic avian data on formulations of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

<u>Mammals</u>

Technical
Utilizing the chronic endpoint (7.2 mg a.i./kg-bw parental toxicity for male rats; equivalent to 100 ppm or mg a.i./kg-diet) from a 2-generation reproduction study (MRID 47701706) conducted with the rat and the T-REX model v.1.4.1, the chronic mammalian *dietary-based* RQs do not exceed the chronic LOC for mammals. However, the chronic mammalian *dose-based* RQs (1.17-3.86) do exceed the chronic LOC (of 1) for mammals for the short grass food item (in all size classes: 15, 35, and 1000g) as well as the tall grass and broadleaf plants/small insects categories (in the smaller two size classes: 15 and 35 g) for a couple of maximum seasonal application rates (0.267 lbs a.i./A, 0.206 lbs a.i./A). LOC exceedances (*i.e.*, RQ of 1.19-1.74) for the short grass food item (in the smaller two size classes: 15 and 35g) occurs for the remaining maximum seasonal application rates (0.120 lbs a.i./A and 0.096 lbs a.i./A). The NOAEL is based on decreased body weight, body weight gain, and food consumption and has implications for survival of the test organism in the long term. Given that LOCs were exceeded for the given maximum *seasonal* applications, chronic risk to mammals <u>is expected</u> as a result of pyroxasulfone use on corn, soybean, winter wheat, fallow land, and non-crop sites. Reducing the maximum seasonal application rate would alleviate the risk concern.

Metabolites/degradates
No chronic mammalian data on metabolites/degradates of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

Formulations
No chronic mammalian data on formulations of pyroxasulfone was provided. Risk cannot be precluded on the basis of no data available.

b. Terrestrial Plants

Utilizing the toxicity endpoints (MRID 47701638 - seedling emergence: monocot EC_{25} = 0.0669 lbs a.i./A, NOAEC = 0.0168 lbs a.i./A and dicot EC_{25} = 0.2615 lbs a.i./A, NOAEC = 0.1338 lbs a.i./A; MRID 47701639 - vegetative vigor: monocot EC_{25} > 0.2676 lbs a.i./A, NOAEC = 0.2676 lbs a.i./A, dicot EC_{25} = 0.0748 lbs a.i./A, NOAEC = 0.0168 lbs a.i./A), assuming liquid ground spray (1% drift fraction) and aerial spray (5% drift fraction) application method, a default incorporation depth of 1 inch, and a solubility limit in water of 3.49 mg/L (at 25°C), the RQ calculations (1.07-1.75), indicate that monocots in semi-aquatic areas (but not in dry areas or as a result of spray drift only areas) exposed to runoff and spray drift from either ground or aerial spray applications are most sensitive given that the listed species LOC (of 1) is exceeded for several maximum *seasonal* application rates (0.267 lbs a.i./A, 0.206 lbs a.i./A for ground spray applications and 0.120 lbs a.i./A for aerial spray applications, see Table 36). Changing the application rate from 0.267 to 0.2136 lbs a.i./A (the maximum single application rate) alters the RQ from 1.75 to 1.40 but does not change the risk conclusion for ground spray applications with KIH-485/Pyroxasulfone W85 formulations. The maximum *seasonal* and maximum single application rate for the V-10233 Herbicide Water Dispersible Granules commercial label is the same (*i.e.*, 0.206 lbs a.i./A); therefore, the RQ calculations and risk conclusions for ground spray applications with this formulation do not change. Similarly, the maximum *seasonal* and maximum single application rate for the V-10233 Herbicide label, which is the only label with proposed aerial spray applications, is the same (*i.e.*, 0.120 lbs a.i./A); therefore, the RQ calculations and risk conclusions specifically regarding aerial spray applications with this formulation do not change. The terrestrial plant studies generally indicated effects on length (height) and/or dry weight; additional effects included chlorosis, necrosis, stem and leaf curl. Given that LOCs were exceeded for the given maximum *seasonal* as well as maximum single applications, risk to terrestrial plants is expected as a result of pyroxasulfone use on corn, soybean, winter wheat, fallow land, and non-crop sites. Reducing the maximum seasonal application rate would alleviate the risk concern.

Risk from contaminated irrigation water
Predicted groundwater concentrations of pyroxasulfone (equivalent to the equilibrium concentration taken over a 30 year period) were used to estimate the potential phytotoxic effects from irrigation water to plants and sensitive crops on the treated field. It is assumed that a one-acre field is irrigated with one inch of water containing pyroxasulfone at the equilibrium concentration. There are no non-listed plant LOC exceedances (on the basis of EEC/ EC_{25}); however, given the estimates for the DE and WI scenarios, listed

plant LOCs are exceeded (on the basis of EEC/NOAEC) with RQs of 1.12 and 2.01 for both monocot and dicot species. Therefore, risk to listed terrestrial plants and potentially sensitive crops located on the irrigated field are expected as a result of use of pyroxasulfone contaminated irrigation water at the estimated levels.

3. Review of Incident Data

With the proposed uses on corn, wheat, soybean, and non-crop sites, pyroxasulfone will be applied in the United States for the first time. Therefore, no incident data are available at this time.

4. Endocrine Effects

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA is issuing test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Pyroxasulfone is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

5. Federally Threatened and Endangered (Listed) Species

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an "action" that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species" (50 C.F.R. § 402.02).

To facilitate compliance with the requirements of the Endangered Species Act (subsection (a)(2)), the Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (USEPA, 2004). After the Agency's screening level risk assessment is conducted, if any of the Agency's listed species LOCs are exceeded for either direct or indirect effects, an analysis is conducted to determine if any listed or candidate species may co-occur in the area of the proposed pesticide use or areas downstream or downwind that could be contaminated from drift or runoff/erosion. If listed or candidate species may be present in the proposed action areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

Both acute endangered species and chronic risk LOCs are considered in the screening-level risk assessment of pesticide risks to listed species. Endangered species acute LOCs are a fraction of the non-endangered species LOCs or, in the case of endangered plants, RQs are derived using lower toxicity endpoints than non-endangered plants. Therefore, concerns regarding listed species within a taxonomic group are triggered in exposure situations where restricted use or acute risk LOCs are triggered for the same taxonomic group. The risk assessment also includes an evaluation of the potential probability of individual effects for exposures that may occur at the established endangered species LOC both in the risk characterization and the endangered species sections. This probability is calculated using the established dose/response relationship and assumes a probit (probability unit) dose/response relationship.

a. Action Area

For listed species assessments, the action area is considered to be the area affected directly or indirectly by the Federal action and not merely the immediate area where pyroxasulfone is applied. At the initial Level 1 screening assessment, broadly described taxonomic groups are considered, and thus, conservatively assumes that listed species within those broad groups are co-located with the pesticide treatment area. This means that terrestrial plants and wildlife are assumed to be located on or adjacent to the treated site and aquatic organisms are assumed to be located in a surface water body adjacent to the treated site. The assessment also assumes that listed species are located within the area of highest exposure to the pesticide, and that exposure will decrease with increasing distance from the treated area.

If the assumptions associated with the screening-level action area result in RQs that are below the listed species LOCs, a "no effect" determination conclusion is made with respect to listed species in that taxa, and no further refinement of the action area is necessary. Furthermore, RQs below the listed species LOCs for a given taxonomic group indicate no concern for indirect effects upon listed species that depend upon the taxonomic group covered by the RQ as a resource. However, in situations where the screening assumptions lead to RQs in excess of the listed species LOCs for a given taxonomic group, a potential for a "may affect" conclusion exists and may be associated with direct effects on listed species belonging to that taxonomic group or may extend to indirect effects upon listed species that depend upon that taxonomic group as a resource. In such cases, additional information on the biology of listed species, the locations of these species, and the locations of use sites could be considered along with available information on the fate and transport properties of the pesticide to determine the extent to which screening assumptions regarding an action area apply to a particular listed organism. These subsequent refinement steps could consider how this information would impact the action area for a particular listed organism and may potentially include areas of exposure that are downwind and downstream of the pesticide use site.

b. Taxonomic Groups Potentially at Risk

The preliminary risk assessment for endangered species indicates that the proposed use and application rate for pyroxasulfone either exceeds the Endangered Species LOCs or may directly affect the following taxonomic groups:

- Terrestrial plants
- Aquatic plants
- Birds (as well as reptiles, terrestrial-phase amphibians)
- Mammals

Table 38. Listed Species Risks Associated With Direct or Indirect Effects from Pyroxasulfone use		
Listed Taxon	**Direct Effects**	**Indirect Effects**
Terrestrial and semi-aquatic plants - monocots	Yes	Yes[4]
Terrestrial and semi-aquatic plants – dicots	No	Yes[4]
Terrestrial invertebrates	No	Yes[4]
Birds	Yes (chronic)	Yes[4]
Terrestrial-phase amphibians	Yes (chronic)	Yes[4]
Reptiles	Yes (chronic)	Yes[4]
Mammals	Yes (chronic)	Yes[4]
Aquatic non-vascular plants	Yes	Yes[4]
Aquatic vascular plants	Yes	Yes[4]
Freshwater (FW) fish	No	Yes[4]
Aquatic-phase amphibians	No	Yes[4]
Freshwater (FW) invertebrates	No	Yes[4]
Marine/estuarine (M/E) fish	No[3]	Yes[4]
Marine/estuarine (M/E) invertebrates (mollusk)	No[3]	Yes[4]

[1] Results from birds used as surrogate for assessing risk to terrestrial-phase amphibians and reptiles
[2] Results from freshwater fish used as surrogate for assessing risk to aquatic-phase amphibians
[3] Assumption of no expected risk or direct effect is made on the basis of freshwater fish and invertebrate data.
[4] From effects to mammals, birds, plants

1. *Discussion of risk quotients*

The Agency's LOCs for terrestrial and aquatic plants, mammals (chronic), and birds (chronic) are exceeded for the use of pyroxasulfone as outlined in previous sections. Should estimated exposure levels occur in proximity to listed resources, the available screening level information suggests a potential concern for direct effects on listed species within the taxonomic groups listed above associated with the uses of pyroxasulfone as described in Section III.A. The registrant must provide information on the proximity of federally listed terrestrial and aquatic plants, mammals, birds, reptiles, and terrestrial-phase amphibians to the pyroxasulfone use sites. This requirement may be satisfied in one of three ways: 1) having membership in the FIFRA Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2); 2) citing FIFRA Endangered Species Task Force data; or 3) independently producing these data, provided the information is of sufficient quality to meet FIFRA requirements. The information will be used by the OPP Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

2. *Probit dose response relationship*

The Agency uses the probit dose response relationship as a tool for providing additional information on the potential for acute direct effects to aquatic and terrestrial animals (U.S. EPA, 2004). As part of the risk characterization, an interpretation of acute RQ for listed species is discussed. This interpretation is presented in terms of the chance of an individual event (i.e., mortality or immobilization) should exposure at the EEC actually occur for a species with sensitivity to pyroxasulfone on par with the acute toxicity endpoint selected for RQ calculation. To accomplish this interpretation, the Agency uses the slope of the dose response relationship available from the toxicity study used to establish the acute toxicity measures of effect for each taxonomic group that is relevant to this assessment. The individual effects probability associated with the acute RQ is based on the mean estimate of the slope and an assumption of a probit dose response relationship. In addition to a single effects probability estimate based on the mean, upper and lower estimates of the effects probability are also provided to account for variance in the slope, if available. The upper and lower bounds of the effects probability are based on available information on the 95% confidence interval of the slope. Studies with good probit fit characteristics (i.e., statistically appropriate for the data set) are associated with a high degree of confidence. Conversely, a low degree of confidence is associated with data from studies that do not statistically support a probit dose response relationship. In addition, confidence in the data set may be reduced by high variance in the slope (i.e., large 95% confidence intervals), despite good probit fit characteristics. In the event that dose response information is not available to estimate a slope, a default slope assumption of 4.5 (95% C.I.: 2 to 9) (Urban and Cook, 1986) is used.

Individual effect probabilities are calculated based on an Excel spreadsheet tool IEC v1.1 (Individual Effect Chance Model Version 1.1) developed by the U.S. EPA, OPP, Environmental Fate and Effects Division (June 22, 2004). The model allows for such calculations by entering the mean slope estimate (and the 95% confidence bounds of that estimate) as the slope parameter for the spreadsheet. In addition, the acute RQ is entered as the desired threshold.

3. *Data related to under-represented taxa*

Effects data on under-represented taxonomic groups were not submitted by the Registrant. Effects data from other analyzed sources were either not obtained (ECOTOX Database, PAN Database) or were not available (publicly available ECOTOX) for this screening risk assessment.

c. Indirect Effects Analysis

In conducting a screen for indirect effects, direct effects LOCs for each taxonomic group are used to make inferences concerning the potential for indirect effects upon listed species. The listed species rely upon non-listed organisms in these taxonomic groups as resources critical to their life cycle. Pesticide-use scenarios, resulting in RQs that are below all direct effect listed species LOCs for all taxonomic groups assessed are considered of no concern for risks to listed species either by direct or indirect effects. However, there may be situations where a taxonomic group is not quantitatively assessed (e.g., some non-guideline terrestrial invertebrates), but other lines of evidence are sufficiently supportive of concerns for indirect effects on listed organisms that are dependant upon that taxonomic group.

- **Where One or More Animal Taxonomic Group RQs Exceed the LOC for Listed Species**

The Level I screening indirect effects analysis documents those types of dependencies upon non-listed organisms that could be important sources of indirect effects to listed organisms should effective levels of the pesticide coincide with locations of listed species and the biologically based resources upon which they depend. In cases where screening-level acute RQs for a given animal group equal or exceed the listed species acute LOC, the Agency uses the dose response relationship from the toxicity study used for calculating the RQ to estimate the probability of acute effects associated with an exposure equivalent to the EEC. This information serves as a guide to establish the need for and extent of additional analysis that may be performed using Services-provided "species profiles" as well as evaluations of the geographical and temporal nature of the exposure to ascertain if a not likely to adversely affect determination can be made. The degree to which additional analyses are performed is commensurate with the predicted probability of adverse effects from the comparison of dose response information with the EECs. The greater the probability that exposures will produce effects on a taxa, the greater the concern for potential indirect effects for listed species dependent upon that taxa, and therefore, the more intensive the analysis on the potential listed species of concern, their locations relative to the use site, and information regarding the use scenario (e.g., timing, frequency, and geographical extent of pesticide application). The greatest concerns would exist when exposure is associated with a risk higher than the effects probability associated with the non-listed LOC for a pesticide with an average slope of 4.5.

For pyroxasulfone, risks to listed species are predicted within the following taxa: terrestrial and aquatic plants, mammals, birds, reptiles, and terrestrial-phase amphibians. For example, given that the chronic LOC is exceeded for mammals, indirect effects to listed species (e.g., other mammals, birds, amphibians, reptiles, plants (pollination)) that rely on mammals as a primary food source, or on mammal burrows for shelter or breeding habitat, may be of concern.

d. Critical Habitat

In the evaluation of pesticide effects on designated critical habitat, consideration is given to the physical and biological features (constituent elements) of a critical habitat identified by the U.S Fish and Wildlife and National Marine Fisheries Services as essential to the conservation of a listed species and which may require special management considerations or protection. The evaluation of impacts for a screening level pesticide risk assessment focuses on the biological features that are constituent elements and is accomplished using the screening-level taxonomic analysis (risk quotients, RQs) and listed species levels of concern (LOCs) that are used to evaluate direct and indirect effects to listed organisms.

The screening-level risk assessment has identified potential concerns for indirect effects on listed species for those organisms dependent upon terrestrial and aquatic plants, mammals, birds, reptiles, and terrestrial-phase amphibians. In light of the potential for indirect effects, the next step for EPA and the Service(s) is to identify which listed species and critical habitat are potentially implicated. Analytically, the identification of such species and critical habitat can occur in either of two ways. First, the agencies could determine whether the action area overlaps critical habitat or the occupied range of any listed species. If so, EPA would examine whether the pesticide's potential impacts on non-listed species would affect the listed species indirectly or directly affect a constituent element of the critical habitat. Alternatively, the agencies could determine which listed species depend on biological resources, or have constituent elements, that fall into the taxa that may be directly or indirectly impacted by the pesticide. Then EPA would determine whether use of the pesticide overlaps the critical habitat or the occupied range of those listed species. At present, the information reviewed by EPA does not permit use of either analytical approach to make a definitive identification of species that are potentially impacted indirectly or critical habitat that is potentially impacted directly by the use of the pesticide. EPA and the Service(s) are working together to conduct the necessary analysis.

This screening-level risk assessment for critical habitat provides a listing of potential biological features that, if they are constituent elements of one or more critical habitats, would be of potential concern. These correspond to the taxonomic groups identified above as being of potential concern for indirect effects. This should serve as an initial step in problem formulation for further assessment of critical habitat impacts outlined above, should additional work be necessary.

e. Co-occurrence Analysis

The goal of the analysis for co-location is to determine whether sites of pesticide use are geographically associated with known locations of listed species. At the screening level, this analysis is accomplished using the LOCATES v. 2.13 database. The database uses location information for listed species at the county level and compares it to agricultural census data for crop production at the same county level of resolution. The product is a listing of federally listed species that are located within counties known to produce the crop upon which the pesticide will be used.

Tables 39 and **40** below report the number of states and counties in which endangered species reside that have the proposed pyroxasulfone uses. The data suggest that there is considerable potential for exposure to a variety of endangered species (1,223 species total) from pyroxasulfone uses. For additional LOCATES output refer to **Appendix G**.

Table 39. Number of Endangered Species Potentially Exposed to Pyroxasulfone with the Proposed Uses											
	Mammals	Amphibians	Birds	Reptiles	Arachnids	Insects	Conf/Cyc	Dicot	Ferns	Lichen	Monocots
Counties	1412	150	1469	398	15	259	8	930	51	22	553
States	68	21	69	31	12	55	3	599	22	2	65
Species	50	13	47	34	5	30	3	47	10	5	46

Table 40. Number of Endangered Species Potentially Exposed to Pyroxasulfone with the Proposed Uses					
	Bivalve	Crustacean	Fish	Gastropod	Marine Mammal
Counties	556	75	872	57	556
States	70	20	114	72	70
Species	30	13	39	18	30

C. Description of Assumptions, Limitations, Uncertainties, Strengths, and Data Gaps

1. Assumptions, Limitations, and Uncertainties Related to Exposure for all Taxa

a. Maximum Use Scenario

The screening-level risk assessment focuses on characterizing potential ecological risks resulting from a maximum use scenario, which is determined from labeled statements of maximum application rate and number of applications with the shortest time interval between applications. The frequency at which actual uses approach this maximum use scenario may be dependant on herbicide resistance, timing of applications, cultural practices, and market forces. Furthermore, this assessment utilizes the maximum *seasonal* application rate for RQ calculation over the maximum single application rate for several reasons. The maximum *seasonal* application rate was used to calculate RQs given that the maximum single application rates were either equal or approximately equal to the seasonal rate. In addition, given that application intervals were not reported on the labels and pyroxasulfone's persistence in water (half-lives ranging from 69 to 119 days) and soil (half-lives ranging from 142 to 533 days), the maximum *seasonal* rate was assumed appropriate for RQ calculations. Nevertheless, in cases where RQs exceeded LOCs, lower application rates were used for risk characterization. Furthermore, the seasonal application rate was assumed to be equivalent to annual application rate.

2. Assumptions, Limitations, and Uncertainties Related to Exposure for Terrestrial Species

a. Location of Wildlife Species

For this screening-level terrestrial risk assessment, a generic bird or mammal was assumed to occupy either the treated field or adjacent areas receiving pyroxasulfone at the treatment rate on the field. Actual habitat requirements of any particular terrestrial species were not considered, and it was assumed that species occupy, exclusively and permanently, the modeled treatment area. Spray drift model predictions suggest that this assumption leads to an overestimation of exposure to species that do not occupy the treated field exclusively and permanently.

b. Routes of Exposure

This screening-level assessment for ground (liquid) applications of pyroxasulfone considered dietary, inhalation, and drinking water exposure. Other routes of exposure that were not considered in the assessment are incidental soil ingestion exposure and dermal exposure.

c. Dietary Intake and Other Limitations of Oral Studies in Terrestrial Species

The avian acute oral study and the avian subacute dietary study each have limitations for estimating the risk to wild species exposed to pesticides in the environment. Both studies have a fixed exposure period and do not allow for differences in the responses of individuals to different durations of exposure. With the acute oral study, the chemical is administered in a single dose. This does not mimic wild bird exposure through multiple feedings. Also, it does not account for the effect of different environmental matrices on absorption rate into the gastrointestinal tract of the animal. With the acute dietary study, the endpoint is reported as the concentration mixed with food that produces a response rather than as the dose ingested. Although food consumption sometimes allows for estimation of a dose, calculations of the mg/kg/day are confounded by undocumented spillage of feed and how consumption is measured over the duration of the test. Usually, if measured at all, food consumption is estimated once at the end of the five-day exposure period. Group housing of birds undergoing testing allows for a measure of only the average consumption per day for a group, and consumption estimates can be further confounded if birds die within a treatment group. In addition, the dietary study utilizes young birds. The exponential growth of young birds complicates the estimate of the dose; controls often nearly double in size over the duration of the test. Since weights are only taken at the initiation and at the end of the exposure period, the dose per body weight (mg/kg) is difficult to estimate with any precision. The interpretation of this test can be further confounded by dietary consumption. Estimation of the acute LC_{50} value is not only a function of the intrinsic toxicity of the pesticide, but also the willingness of the birds to consume treated food.

In addition to the uncertainties associated with the two toxicity studies utilized for estimating acute risk to birds, other factors, not normally taken into account in a screening level risk assessment may narrow the differences between the dose-based and dietary-based acute RQs for birds. The factors include differences in gross energy and assimilative efficiency of laboratory feed versus food items in the field, basic maintenance metabolic rates between wild birds and captive birds, seasonal free living dietary requirements for wild birds (including gorging behavior) and specific food avoidance behavior. These uncertainties may either overestimate or underestimate the risk in a screening level assessment.

Gross Energy and Assimilative Efficiency. This screening level risk assessment does not allow for gross energy and assimilative efficiency differences between wildlife food items and laboratory feed. For example, a typical laboratory avian feed, as used, contains approximately 2750 kcal/ kg. The Agency's Wildlife Exposure Factors Handbook (U.S. Environmental Protection Agency, 1993) presents the following dry-weight and fresh weight caloric contents for selected wildlife food items:

Food Item	Energy Dry (kcal/kg)	Energy Fresh (kcal/kg)
grasses	4200	1300
broadleaf forage	4200	2200
seeds	5100	4700
fruits	2000	1100
insects	5600	1600

On gross energy content alone, direct comparison of a laboratory dietary concentration-based effects threshold to a fresh-weight pesticide residue estimate would result in an underestimation of field exposure by food consumption by a factor of 1.25 - 2.5 for most food items. Only for seeds would the direct comparison of dietary threshold to residue estimate lead to an overestimate of exposure.

Depending upon species and dietary matrix, bird assimilation of wild diet energy ranges from 23 - 80%, and mammal's assimilation ranges from 41 - 85% (U.S. EPA, 1993). If it is assumed that laboratory chow is formulated to maximize assimilative efficiency (e.g., a value of 85%), a potential for underestimation of exposure may exist by assuming that consumption of food in the wild is comparable with consumption during laboratory testing.

Metabolic Rates. In the screening process, exposure may be underestimated because metabolic rates are not related to food consumption. For example, the Wildlife Exposure Factors Handbook (U.S. EPA, 1993) includes allometric models for estimating both existing metabolic rate (EMR) and free living metabolic rate (FMR). EMR is the metabolic rate necessary for animal maintenance in captivity without body weight loss, a condition similar to caged test animals. FMR is the energy requirement for an organism in the wild. For passerine birds these relationships are as follows:

$$\text{EMR (kcal/day)} = 1.572\ (\text{body weight g})^{0.6210}$$
$$\text{FMR (kcal/day)} = 2.123\ (\text{body weight g})^{0.749}$$

Using a weight range for passerines of 10 - 150 g, the EMR predictions range from 6.6 to 35.3, and the FMR ranges from 11.9 to 90.5 kcal/day. Thus, it appears that not accounting for increased energy demands of organisms in the wild when comparing dietary residues to dietary toxicity thresholds represents about a two-fold underestimation in exposure potential.

Free Living Metabolic Requirements. The screening procedure does not account for situations where the feeding rate may be above or below requirements to meet free living metabolic requirements. Gorging behavior is a possibility under some specific wildlife scenarios (e.g., bird migration) where the food intake rate may be greatly increased. Kirkwood (1983) has suggested that an upper-bound limit to this behavior might be the typical intake rate multiplied by a factor of 5.

Avoidance. In contrast is the potential for avoidance, operationally defined as animals responding to the presence of noxious chemicals in their food by reducing consumption of treated dietary elements. This response is seen in nature where herbivores avoid plant secondary compounds. For agrochemicals, Dolbeer *et al.* (1994) reported that the use of methiocarb on fruit crops reduced depredation by birds. Of course, chemical treatment of food sources and any subsequent avoidance of those food sources by a species may, in itself, result in detrimental effects on the energetics of the species.

d. Incidental Releases Associated with Use

This risk assessment was based on the assumption that the entire treatment area is subject to pesticide application at the rates specified on the label. Uneven application of the pesticide through changes in calibration of application equipment, spillage, and localized releases at specific areas of the treated field that are associated with specifics of the type of application equipment were not accounted for in this assessment.

e. Residue Levels Selection

The Agency relies on the work of Fletcher et al. (1994) for setting the assumed pesticide residues in wildlife dietary items. These residue assumptions are believed to reflect a realistic upper-bound residue estimate, although the degree to which this assumption reflects a specific percentile estimate is difficult to quantify. It is important to note that the field measurement efforts used to develop the Fletcher estimates of exposure involve highly varied sampling techniques. It is entirely possible that much of these data reflects residues averaged over the entire above ground plants in the case of grass and forage sampling. Depending upon a specific wildlife species' foraging habits, whole aboveground plant samples may either underestimate or overestimate actual exposure.

f. TerrPlant Model

At this time, the TerrPlant model cannot accurately estimate terrestrial exposure levels with pesticides applied with multiple applications or application intervals. The technology is not yet available for these types of estimations. The maximum *seasonal* application rate was used to calculate RQs given that the maximum single application rates were either equal or approximately equal to the seasonal rate. In addition, given that application intervals were not reported on the labels and pyroxasulfone's persistence in water (half-lives ranging from 69 to 119 days) and soil (half-lives ranging from 142 to 533 days), the maximum *seasonal* rate was assumed appropriate for RQ calculations. Nevertheless, in cases where RQs exceeded LOCs, lower application rates were used for risk characterization. Furthermore, the seasonal application rate was assumed to be equivalent to annual application rate.

3. Assumptions, Limitations, and Uncertainties Related to Effects Assessment

a. Sublethal Effects

For an acute risk assessment, the screening risk assessment relies on the acute mortality endpoint as well as a suite of sublethal responses to the pesticide, as determined by the testing of species response to chronic exposure conditions and subsequent chronic risk assessment. Consideration of additional sublethal data in the assessment is exercised on a case-by-case basis and only after careful consideration of the nature of the sublethal effect measured and the extent and quality of available data to support establishing a plausible relationship between the measure of effect (sublethal endpoint) and the assessment endpoints.

b. Age Class and Sensitivity of Effects Thresholds

Testing of juvenile organisms may overestimate toxicity at older age classes for pesticidal active ingredients that act directly (without metabolic transformation) because younger age classes may not have the enzymatic systems associated with detoxifying xenobiotics. However, the influence of age may not be uniform for all compounds, and compounds requiring metabolic activation may be more toxic in older age classes. The risk assessment uses the most sensitive life-stage information as the conservative screening endpoint.

c. Use of Most Sensitive Species Tested

Screening risk assessment relies on a selected toxicity endpoint from the most sensitive species tested; however, the selected toxicity endpoints do not necessarily reflect sensitivity of the most sensitive species in a given environment. The relative position of the most sensitive species tested in the distribution of all possible species is a function of the overall variability among species to a particular chemical. Toxicity thresholds may vary up to four orders of magnitude across species for some chemicals[4]. Therefore, risk conclusions may under- or overestimate actual ecological risk for a given species.

4. Assumptions, Limitations, Uncertainties, Strengths, and Data Gaps Related to the Acute and Chronic LOC's

The risk characterization section of the assessment document includes an evaluation of the potential for individual effects to listed species at an exposure level equivalent to the LOC. This evaluation is based on the median lethal dose estimate and dose/response

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4 Mayer, F.L. and M.R. Ellersieck, 1986. Manual of acute toxicity: Interpretation and data base for 410 chemicals of freshwater animals. Resource Publication 160. U. S. Fish and Wildlife Service. Department of the Interior, Washington, D.C., 579 p.

relationship established for the effects study corresponding to each taxonomic group for which the LOCs are exceeded. The slope of the probit-dose response is used to generate a probability of individual effects near the low end tail of the curve. Predictions based on low probability events are by nature highly uncertain. Moreover, for this assessment the dose-response curve representing a given taxa is generated from one study using one species. It is likely that the resulting dose-response relationship does not represent the response of all species within a taxa. Calculating the probability of individual effects at the lower and upper bounds of the slope is designed to address this source of uncertainty but the extent to which this captures the variability within a taxa is unknown. In some cases, a probit dose-response relationship cannot be calculated. In these instances, event probabilities are calculated based on a default slope assumption of 4.5 (Urban and Cook, 1986).

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